

SIMPLIFIED GYNECOLOGY

**Obstetrics and Gynecology Department
Zagazig University**



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Preface

Welcome to this edition of "Simplified Gynecology", a book for medical students, nursing students as well as those in the early part of their professional careers. This edition reflects the changes in practices that have taken place in woman's health care and implements the guidelines from important scientific bodies as the Royal College of Obstetrics and Gynecology.

Feedback from the medical students had led us to make big modification of the book as some subjects had been expanded while other less relevant topics had been omitted or reduced.

I wish to express my greatest thanks and gratitude to a group of colleagues in the Department of Obstetrics and Gynecology, Zagazig University, at different grades from professors and lectures through very enthusiastic and promising assistant lectures who had spent a lot of their time and efforts to produce this book in its final form. Having done this big effort, they requested their names not to be acknowledged in the book and regarded this contribution as an integral part of their profession and their commitment towards their students and Patients.

We hope this book will improve the ability of the medical students to understand the basic subjects of Gynecology as well as the young professionals to get a rapid but a complete review of the subject. We are very happy to receive your comments and feedback that will help us to improve future editions of this book.

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I. Basic Gynecology

Anatomy The external genital organs

The vulva means the female external genital organs and is composed of the following structures:

Mons pubis (Mons veneris):

Mass of fat overlies the symphysis pubis; covered by skin and hair.

NB: Pubic hair may be:

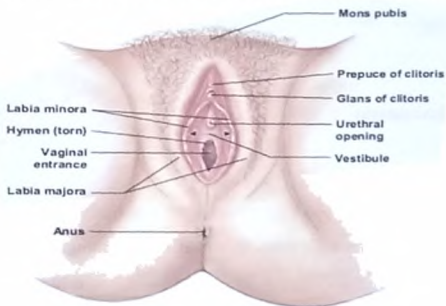
- Feminine with upper straight border.
- Masculine with upper convex border.

Labia majora:

- Two skin folds anteriorly unite with mons pubis and posteriorly unite with skin of perineum and join each other forming posterior commissure.
- Each labium major contains mass of fat.
- The skin is covered with hair and contains sebaceous and sweat glands.

NB: Some of sweat glands are large and coiled known as apocrine glands. Their secretion gives characteristic odor.

- Each labium major has 2 surfaces:
 - Medial:** Less pigmented and smooth.
 - Lateral:** More pigmented and covered by hair.
- Round ligament is inserted in the upper part of the labium major.



Labia minora (nymphae):

- Two skin folds lying within labia majora.
- Each labium minor contains loose connective tissue, devoid of fat and is very vascular. So, it becomes turgid during sexual excitement.
- The skin is non-keratinized containing sebaceous glands but no hair nor sweat glands.
- Anteriorly, each labium minor divides into 2 flaps:
 - Upper flaps unite above the clitoris to form prepuce of clitoris.
 - Lower flaps unite to form frenulum of clitoris.
- Posteriorly, they unite to form sharp fold of skin called Fourchette.
- Fossa navicularis is the depression between Fourchette and hymen.

I. Basic Gynecology

Clitoris:

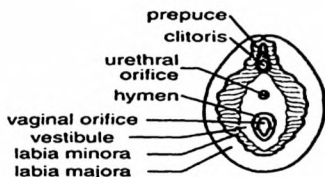
- Homologous to penis in male.
- Lies in front of symphysis pubis and attached to it by suspensory ligament.
- It is 1-2 cm in length and has:
- Body formed of 2 corpora cavernosa.
- Glans formed of erectile tissue.
- The most sensitive part of vulva as it is richly supplied with nerves.

NB: Clitoromegaly is enlargement of clitoris and occurs in cases of hyperandrogenism.

- Removal of clitoris (during circumcision) → decrease sexual desire

Vestibule:

- Area lying within labia minora.
- It receives opening of:
 - External urethral meatus.
 - Vaginal orifice.
 - Bartholin glands.
 - 4-Minor vestibular glands.



External urethral meatus:

- About 2.5 cm below clitoris.
- Skene tubules (two paraurethral ducts) open in the floor of urethra 1 cm from external urethral meatus.
- Length of female urethra 4 cm.

Vaginal orifice:

- Bounded by:
 - **Anteriorly:** External urethral meatus.
 - **Posteriorly:** Fourchette.
 - **Laterally:** Labia minora.
- In virgins, it is partially closed by hymen.

Hymen:

- Fold of mucous membrane, covered on both sides by stratified squamous epithelium.
- It has one or more openings to allow passage of menstrual blood.
- It may be:
 - annular,
 - crescentic,
 - biperforate (septate),
 - cribriform or
 - imperforate (result in cryptomenorrhea).



- After first coitus, hymen is torn unless it is abnormally elastic.
- During delivery, hymen is destroyed leaving small tags of fibrous tissue (carunculae myritiformes or hymenalis).

Bulbs of vestibule:

- Two elongated masses of erectile tissue; one on each side of vaginal orifice.
- Covered by bulbocavernosus muscles.

I. Basic Gynecology

Bartholin glands (greater vestibular gland):

- **Number:** Two
- **Size:** Small (one cm).
- **Shape:** Oval glands.
- **Site:** Embedded in the posterior part of the vestibular bulb.
- **Structure:**
 - It is a compound racemose gland.
 - The acini are lined by columnar epithelium.
 - The duct (one inch), lined by transitional epithelium, open in the vestibule at 5 and 7 O'clock position.
- **Function:** Produces mucoid secretion in response to sexual excitement acting as a lubricant for coitus.
- The gland is not felt unless diseased and the duct opening not seen unless inflamed.



Blood supply :

Arterial:

-**External pudendal artery:** Branch of femoral artery.

-**Internal pudendal artery:** One of the two terminal branches of the internal iliac artery.

Venous drainage:

-Accompany corresponding arteries.

-Venous drainage of clitoris joins vaginal and vesical plexuses of veins.

Nerve supply:

1. Pudendal nerve ($S_2, 3, 4$).
2. Ilio-inguinal nerve.
3. Genital branch of genitofemoral nerve.
4. Posterior cutaneous nerve of the thigh.

Lymphatic drainage:

- **Inguinal** (superficial and deep) and **femoral** (superficial and deep) lymph nodes on both sides because there is crossing of lymphatics.
- Then from deep femoral lymph node (**lymph node of Cloquet or Rosenmuller**) that present in femoral canal to external iliac LN → Common iliac LN → Para-aortic LN.

NB: Clitoris drains directly into deep femoral LN

Perineum

Anatomical (true) perineum :

The region which overlies the pelvic outlet which is diamond-shaped. It is divided into:

(1) Anterior (urogenital) triangle: Covered by the vulva and contains:

1. Superficial perineal pouch.
2. Perineal membrane.
3. Deep perineal pouch.

(2) Posterior (anal) triangle: Contains:

1. Anal canal surrounded by external anal sphincter.
2. Ischio-rectal fossa (one on each side).

I. Basic Gynecology

Gynecological perineum:

It is the area between posterior commissure and the anus (2.5 cm or more). It is formed of:

1. Perineal skin (less hairy).
2. Subcutaneous tissue.
3. Perineal body.

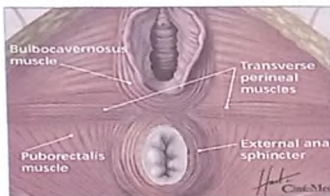
Perineal body:

Fibromuscular mass that gives attachment to the following muscles:

1. Levator ani muscle on both sides.
2. Superficial transverse perinii muscles.
3. Deep transverse perinii muscles.
4. Bulbospongiosus muscle.
5. Part of external anal sphincter.
6. Part of external urethral sphincter.

Functions:

1. Shares in support of pelvic organ.
2. Essential for integrity of pelvic floor.



Internal genital organs Vagina

- It is fibromuscular tube extending upwards and backwards from the vulva to the uterus.
- It forms an angle of 60 degrees with the horizontal plane.
- Vaginal fornices: Entrance of cervix into upper part of vagina divides it into:

- Anterior fornix (shallow).
- Posterior fornix (deep).
- Two lateral fornices.

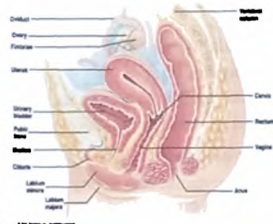
Relations:

Anterior wall (3 inches):

- Upper third → pierced by the cervix.
- Middle third → base of urinary bladder.
- Lower third → urethra.

Posterior wall (4 inches):

- Upper third → covered by peritoneum of Douglas pouch.
- Middle third → the lower third of rectum.
- Lower third → perineal body.



Laterally: From above downwards:

1. Crossing of uterine artery over ureter (2 cm lateral and above lateral fornix).
2. MacKenrods ligament.
3. Pelvic connective tissue.
4. Levator ani muscle.
5. Deep perineal pouch.
6. Bulb of vestibule.
7. Bulbocavernosus muscle.
8. Bartholin gland.

I. Basic Gynecology

Histology:

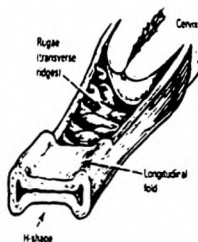
Mucosa:

- Lined by stratified squamous epithelium (non-keratinized).
- Contains glycogen that converted to lactic acid by lactobacilli.
- Reaction of vagina → acidic.
- Estrogen stimulates deposition of glycogen into vagina.
- Contains no glands (if present → vaginal adenosis).
- It is kept moist by vaginal transudate and by cervical secretions.

Submucosa

Musculosa: Inner circular, outer longitudinal smooth muscles.

Sheath of connective tissue.



Support of vagina:

- **Upper vaginal support (level I):** Paracolpium.
- **Midvaginal support (level II):** Endopelvic fascia.
- **Distal vaginal support (level III):** The strongest vaginal support. Distal third of vagina is attached directly to surrounding structure:
 1. **Anterior:** Fused with urethra.
 2. **Posterior:** Perineal body.
 3. **Laterally:** Pupovaginalis muscle.

Blood supply:

Arterial:

Mainly:

- Vaginal artery from internal iliac.
- Cervical branch of uterine artery.

Additionally:

- Middle rectal artery.
- Inferior rectal artery.
- Internal pudendal artery.

Venous drainage: Vaginal venous plexus.

Lymphatic drainage:

Upper two thirds: Similar to that of uterus.

Lower one third: Similar to that of vulva.

Nerve supply:

Upper 4/5: Autonomic (sympathetic-parasympathetic).

Lower 1/5: Pudendal nerve (S_{2,3,4}).

Uterus

It is pear shaped, thick walled hollow muscular organ.

Dimensions:

- In nullipara, 1 x 2 x 3 inches
- In multipara, 1.5 x 2.5 x 3.5 inches

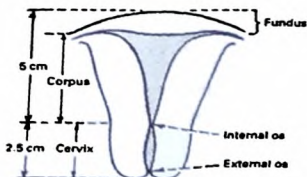
Weight:

- In nullipara, 50 gm
- In multipara, 70 gm

Parts:

Body (2 inches):

- The part above internal os.
- Cornu is the area of insertion of Fallopian tube, round ligament and ovarian ligament.
- Fundus is part of body above the insertion of Fallopian tube.



I. Basic Gynecology

Isthmus (5 mm):

- It lies between anatomical internal os above and histological internal os (the junction of uterine mucosa and cervical mucosa) below.
- It is lined by modified endometrium with few short glands.
- During pregnancy, enlarges forming lower uterine segment (10 cm at term).

Cervix (one inch):

- Has spindle-shaped canal which communicates above with the uterine cavity and below with vagina.
- Divided by entrance of vagina into supra-vaginal part and portio-vaginalis.
- External os is rounded in nullipara and slit shaped in multipara.

- Normally: Uterus: Cervix

2: 1 in adult females

1: 1 in adolescents

1: 2 in infants

* Uterine index:

$$\text{Uterine index} = \frac{\text{length of uterus} - \text{length of CX}}{\text{length of cervix}} \times \frac{1}{2} = \frac{7.5 - 2.5}{2.5} \times \frac{1}{2} = \frac{5}{2.5} \times \frac{1}{2} = 1$$

- Normally, it equals 1 or more.

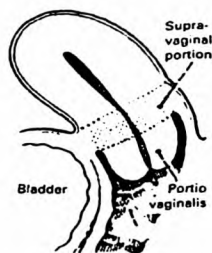
- If $< 0.75 \rightarrow$ hypoplasia of uterus.



Nulliparous os



Parous os



Position of uterus:

- With bladder empty, uterus occupies a central position in the pelvis and the external os at the level of ischial spines.
- Normally, the uterus is anteverted anteflexed (AVF):
 - **Anteverted:** Cervix makes an angle 90° with vagina.
 - **Anteflexed:** Body of uterus makes an angle 160° within cervix.

Causes of AVF:

1- Growth of posterior wall $>$ anterior wall.

2- Uterosacral ligament.

3- Round ligament.

4- Weight of abdominal organs.

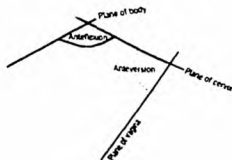
- In about 15% of normal women, the uterus is retroverted or retroflexed or both (retroversion – flexion = RVF).

Support of uterus:

1- Cervical ligament.

2- Pelvic floor.

3- AVF position.



I. Basic Gynecology

Peritoneal covering:

- Body is covered by peritoneum anteriorly and posteriorly.
- From the anterior surface, peritoneum is reflected on the bladder dome to form uterovesical pouch.
- From the posterior surface, peritoneum is reflected on the rectum to form Douglas pouch or cul de sac.

Relations:

- **Anteriorly:** Urinary bladder and uterovesical pouch.
- **Posteriorly:** Douglas pouch containing loops of intestine.
- **Laterally:** Broad ligament and its content including the ureter (2 cm lateral to the cervix).

Histology of uterus :

Endometrium:

- Made of glands and stroma.
- Show cyclic changes.

Myometrium: Three layers of plain muscle fibres:

- Inner circular.
- Intermediate oblique (criss-cross) → control bleeding.
- Outer longitudinal.

Perimetrium (peritoneal coat).

Histology of cervix:

1. **Endocervix** is lined by tall columnar epithelium (secrete alkaline cervical mucus). Below it, there is a layer of cubical (reserve) cells. It contains grooves and crypts referred to as compound racemose glands (liable to chronic infection).

2. **Muscle layer** is inner circular, outer longitudinal.

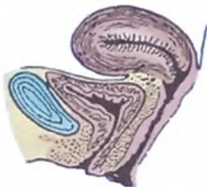
3. **Ectocervix:** Portiovaginalis is covered by stratified squamous epithelium. Junction between endocervix and ectocervix is called Transformation Zone (TZ).

Blood supply :

Arterial :

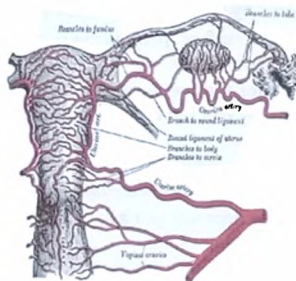
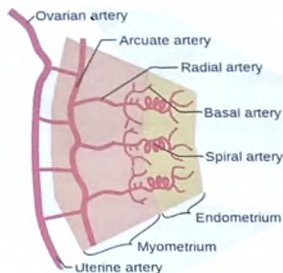
(a) Uterine artery:

- **Origin:** Anterior division of internal iliac artery.
- **Course and relation:**
 - Runs below base of broad ligament.
 - Crosses over ureter 2 cm lateral to cervix.
 - Ascends between 2 layers of broad ligament lateral to uterus "tortuous course".
 - It curves laterally when reach cornu.
- **Ends by anastomosis with ovarian artery.**
- **Branches:**
 - Branches to:
 - * Uterus → coronary branches that give arcuate vessels which continue as radial branches. This radial branch end by dividing into basal and spiral arterioles.
 - * Cervix → Circular artery and descending cervical artery.
 - * Tube and ovary.



I. Basic Gynecology

- Branches to ureter, bladder and upper vagina.



(b) Ovarian artery:

- **Origin:** Abdominal aorta at level of L₃.
- Descends on posterior abdominal wall.
- Enters infundibulopelvic ligament → broad ligament → mesovarian → hilum of ovary.
- Gives anastomotic branches with uterine artery.

Venous drainage :

Pampiniform plexus of veins between 2 layers of broad ligament that drain into:

- Uterine vein → Internal iliac vein.
- Ovarian vein; right → IVC left → left renal vein.

Lymphatic drainage:

Fundus : Para-aortic lymph nodes via ovarian vessels.

Cornu: Inguinal lymph nodes via lymphatics of round ligament.

Middle part of uterus: Internal iliac lymph node.

Lower part of uterus, isthmus and cervix :

- **Primary groups:**
 - * Paracervical, parametrial LN
 - * Internal iliac LN
 - * Obturator LN
 - * External iliac LN
- **Secondary groups:**
 - * Common iliac → para-aortic LN
 - * Sacral LN.

Nerve supply:

Sympathetic:

- **Motor:** T₅₋₆.
- **Sensory:** T_{10, 11, 12, L1}.

Parasympathetic:

 S_{2, 3, 4}.

NB: Cervix is sensitive to dilatation, uterus is sensitive to distension. Both are insensitive to burn, cutting, touch and freezing.

Ligaments of the uterus: It can be:

- **False ligaments (peritoneal folds)** e.g. broad ligament.

- **True ligaments (condensation of endopelvic fascia):**

- 1- Round ligament.
- 2- Ovarian ligament.
- 3- Cervical ligaments.

I. Basic Gynecology

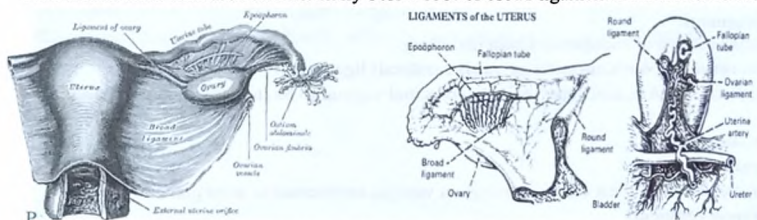
(1) Broad ligament:

1- Fold of peritonum between side of the uterus and lateral pelvic wall.

2- Content :

- Fallopian tube.
- Two ligaments (round and ovarian).
- Two arteries (uterine and ovarian).
- Two veins (uterine and ovarian).
- Embryological remnants (remnants of mesonephric duct "Wolffian system"):
 - Epophoron.
 - Gartner duct.
 - Paroophoron.
 - Koblitz tubule.
- - Parametrium (connective tissue).
- - Nerves.
- - Lymphatics.
- - Venous plexus.

NB: Ureter runs forwards and medially below root of broad ligament 2 cm lateral to cervix.



1. **Infundibulopelvic ligament:** Upper lateral part of broad ligament.
2. **Mesovarium:** Peritoneal fold connecting the ovary to the posterior layer of broad ligament.
3. **Mesosalpinx:** The part between tube and mesovarium.
4. **Mesometrium:** The remaining greater part.

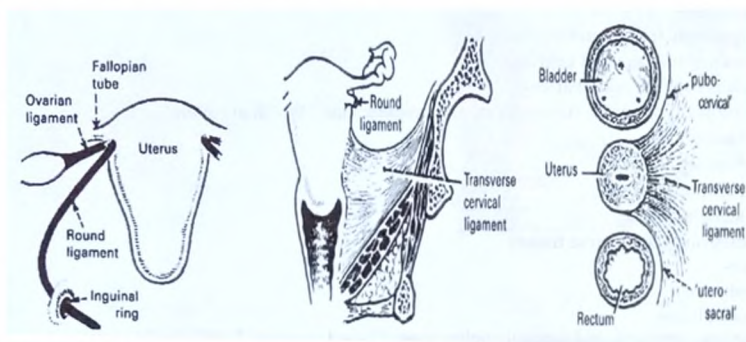
(2) Round ligaments:

- Fibromuscular cords each attached to cornu of uterus in front of tube.
- Passes within broad ligament then through inguinal canal.
- Inserted in the upper part of labium major.
- Arterial supply:
 - Sampson artery (from ovarian artery).
 - Branch from inferior epigastric artery.

I. Basic Gynecology

(3) Ovarian ligaments:

Two fibromuscular cords attached to cornu of uterus behind tube and lower pole of ovary.



(4) Cervical ligaments:

They are condensation of endopelvic fascia including:

- **Transverse cervical (MacKenrodt's or vault cardinal) ligament:**
 - Extends from lateral side of supravaginal cervix and vaginal to be inserted in lateral pelvic wall.
 - It is fan shaped.
- **Uterosacral ligament:**
 - Extends from supravaginal cervix and vaginal vault to be inserted in third piece of sacrum.
- **Puobocervical ligament:**
 - Extends from supravaginal cervix and vaginal vault to be inserted in the back of symphysis pubis.

Fallopian tube

- Extends from cornu of uterus to the ovary (10 cm long).
- Runs in the free border of broad ligaments.

Parts :

- **Interstitial portion (1 cm):** The narrowest part, lies within uterine wall.
- **Isthmus (2-3 cm):** The part immediately lateral to the uterus.
- **Ampulla (5 cm):** The widest part.
- **Infundibulum (fimbriated end):** It has an opening (the abdominal ostium) which is surrounded by number of finger-like processes (fimbriae), the longest one is fimbria ovarica.



I. Basic Gynecology

Histology :

- 1- Endosalpinx** lined by columnar epithelium (secretory cells and ciliated cells).
- 2- Muscle layer:** Inner circular and outer longitudinal.
- 3- Serosa:** Tube covered by peritoneum except lower border.

Function of tube:

- 1- Pickup ovum.
- 2- Transport of ovum.
- 3- Nutrition of ovum.
- 4- Site of fertilization.

Blood supply:

Arterial:

- Uterine artery.
- Ovarian artery.

Tube has double blood supply. So, gangrene never occurs.

Venous drainage:

- Uterine vein.
- Ovarian vein.

Lymphatic drainage :

- 1-** Para-aortic lymph nodes via ovarian lymphatics.
- 2-** Most medial part → inguinal lymph node via lymphatics around round ligaments.

Nerve supply:

- 1- Sympathetic → T₁₁₋₁₂.
- 2- Parasympathetic.

I. Basic Gynecology

The Ovary

- It is oval solid intraperitoneal structure.
- During reproductive years, it measures 1.5 x 2.5 x 3.5 cm.
- In nulliparous women, it lies in a depression on the lateral pelvic wall (ovarian fossa) which is bounded by:
 - **In front**, obliterated umbilical artery.
 - **Behind**, ureter and internal iliac artery.
 - **The floor** of ovarian fossa is formed by: obturator internus muscle, obturator nerves and obturator vessels.

Relations :

Upper pole: Directed upwards and attached to infundibulopelvic ligament.

Lower pole: Directed downwards and attached to ovarian ligament.

Anterior border: Attached to posterior layer of broad ligament by mesovarium.

Posterior border: Free.

Medial wall: Related to intestine.

Lateral wall: Related to peritoneum of ovarian fossa.

Function:

Production of ova.

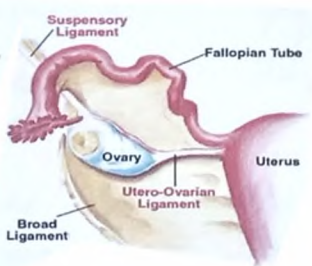
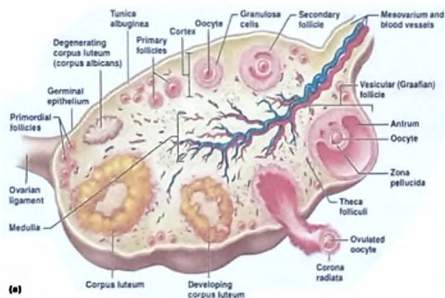
Production of hormones (estrogen, progesterone and androgen).

Histology:

Hilum: Area attached to mesovarium, through which blood vessels, nerves and lymphatics pass.

Medulla: Inner part consists of fibromuscular tissue and blood vessels.

Cortex: Outer part contains ovarian follicles and is covered by connective tissue capsule (tunica albuginea). Single layer of cubical cells (germinal epithelium) covers the tunica.



Blood supply:

Arterial supply:

- Ovarian artery (from aorta just below origin of renal artery).
- Ovarian branch of uterine artery.

Venous drainage:

- Ovarian vein (right → IVC, left → left renal vein).
- Uterine vein → internal iliac vein.

I. Basic Gynecology

Lymphatic drainage: Para-aortic lymph nodes.

Nerve supply:

- Sympathetic → T₁₀₋₁₁.
- Parasympathetic → S_{2, 3, 4}.

NB: Ovaries and fallopian tubes constitute the uterine adnexa.

Pelvic floor

It consists of the following structures from above downwards.

1) Pelvic peritoneum.

2) Endopelvic fascia which includes:

- Parietal fascia: Obturator fascia, piriformis fascia and fascia of pelvic diaphragm.
- Visceral fascia:
 - Encloses extraperitoneal parts of pelvic organs.
 - Its condensation form ligaments.

3) Levator ani muscles which forms pelvic diaphragm.

4) Perineal muscles:

- Superficial transverse perineal muscles.
- Deep transverse perineal muscles.
- Bulbocavernosus muscles.
- Ischiocavernosus muscles.
- External anal sphincter.

5) Subcutaneous fat and fascia.

6) Perineal skin.

Levator ani muscle: It is composed of three parts:

1) Pubococcygeus:

- It arises from back of body of pubic bone and meets its fellow of opposite side in the middle line.
- It is pierced by urethra, vagina and rectum.
- Some fibers are inserted into:
 - Urethra → Pubourethralis.
 - Vagina → Pubovaginalis.
 - Rectum → Puborectalis.
- The remaining fibers are inserted into side of coccyx and ano-coccygeal raphe → pubococcygeus proper.
- Fibers that decussate between vagina and rectum → Fibers of Lushka.
- Fibers that decussate between vagina and urethra → Fibers of Bolkagoff.

2) Iliococcygeus:

- It arises from white line (thickened line on obturator fascia extend from back of pubis to ischial spine).
- It is inserted into side of coccyx.

3) Ischiococcygeus:

- It arises from ischial spine.
- It is inserted into side of coccyx and last piece of sacrum.
- Nerve supply:

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- Superior surface: Perineal branch of S4.
- Inferior surface: Inferior rectal nerve (from pudendal nerve).
- Action:
 - Responsible for internal rotation of head during Support pelvic organs (bladder, vagina, uterus and rectum).
 - Sphincteric action for urethra, vagina and rectum.
 - labour.

NB: Injury of levator ani muscle predisposes to genital prolapse and stress urinary incontinence.

Relations:

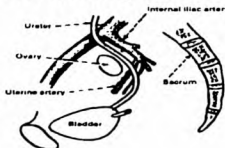
- Superior surface:
 - Covered by pelvic fascia.
 - Related to pelvic organs (bladder, uterus and rectum).
- Inferior surface:
 - Covered by pelvic fascia.
 - Related to ischiorectal fossa.
- Anterior border of both muscles
 - Separated by gap transmitting urethra and vagina.

Pelvic ureter

- Length is 12-15 cm (about the same length of abdominal part).
- Diameter is 3 mm.
- Embryology: It arises from ureteric bud from mesonephric duct.
- Course and relations:
 - It enters the pelvis by crossing the end of the common iliac artery.
 - It runs downwards anterior to internal iliac artery and behind ovarian fossa.
 - When it reaches ischial spine, it runs forwards and medially towards the bladder passing in the base of the broad ligament in ureteric canal and below uterine artery (water under the bridge).

NB: In the later part of its course, the ureter lies 2 cm lateral to the cervix and 2 cm above the vaginal vault.

- Blood supply:
 - Branch from either internal iliac artery, common iliac artery or lower end of aorta.
 - It also receives branches from:
 - 1. Uterine artery.
 - 2. Vaginal artery.
 - 3. Middle rectal artery.
 - 4. Superior vesical artery.



- Dangerous sites for ureteric injury:
 - At pelvic inlet: During clamping of infundibulo-pelvic ligament.
 - Lateral to uterosacral ligament: During clamping of uterosacral ligament.
 - Lateral to vaginal fornices: During clamping of vaginal angle.
 - In the base of broad ligament: During excision of broad ligament tumor.
 - In the parametrium: During excision of parametrium.
 - Along pelvic course: During Wertheim's operation.

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Operations associated with ureteric injury:

- Abdominal hysterectomy.
- Vaginal hysterectomy.
- Wertheim's operation.
- Myomectomy of cervical and broad ligament fibroid.
- Presacral neurectomy (LUNA).
- **Types of injury:**
 - Complete transection.
 - Crushing by clamp.
 - Partial transection.
 - Avascular necrosis.
- **Intraoperative diagnosis:**
 - Transection: Urine in the field with urineferous odor.
 - Ligation: Distension of ureter above site of ligation.
 - This can be confirmed by ureteric catheterization. However, the conditions may be passed undiagnosed.
- **Complications of untreated cases:**
 - Urinoma formation.
 - Peritonitis.
 - Renal failure.
- **Methods for protection of ureter during pelvic surgery:**

Preoperative:

- IVP: Identify course of ureter.
- Ureteric catheter: Allow palpation of ureter.

Intraoperative:

- Exposure of ureter at pelvic brim and its course is followed downwards (ureter is white, cord-like structure with characteristic peristaltic movement).
- Pedicles and ligaments are clamped under vision.
- Subcapsular removal of cervical fibroid.

NB: Branches of internal iliac artery:

Anterior division:

Visceral branches:

- Uterine artery.
- Superior vesical artery.
- Vaginal artery (inferior vesical).
- Middle rectal artery.

Parietal branches:

- Obturator artery.
- Inferior gluteal artery.
- Internal pudendal artery.

Posterior division: All are parietal branches:

- Ilio-lumbar artery.
- Lateral sacral artery.
- Superior gluteal artery.

Embryology of female genital organs

Development of the ovary :

It passes through 2 stages:

I. Indifferent stage:

Extends till 7th week gestation; during which, the ovary and testis are similar histologically although they are genetically determined.

- **Genital ridge:** It is a thickening in the coelomic epithelium between dorsal mesentery and mesonephros at level of T₁₀₋₁₁. Coelomic epithelium proliferates to form sex cords. It undergoes deepening till the upper ends are fused together.
- **Mesenchymal connective tissue** that gives rise to stroma, migrate from nearby the mesonephros to reach the genital ridge.
- **Primitive germ cells** that give rise to ova, develop in the yolk sac, then migrate to the genital ridge (3rd week gestation).

II. Differentiation of the ovary:

- After 7th week gestation.
- An incomplete fibrous capsule "**tunica albuginea**" separates coelomic epithelium from sex cords.
- Sex cords in medulla degenerate and replaced by vascular connective tissue.
- Sex cords in cortex are divided by connective tissue septa to form primary follicles.
- Each primary follicle consists of one primitive germ cell "oogonium" and single layer of flat cells "follicular cells".

Descent of the ovary :

The ovaries develop in the abdomen, then they descend to reach pelvis by:

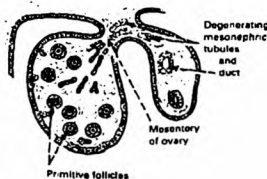
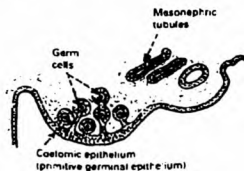
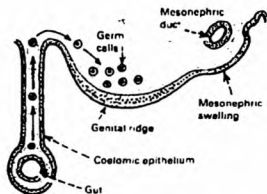
I. Gubernaculum:

- Fibromuscular band extends from lower pole of ovary and labia majora.
- Contraction of gubernaculum → descent of ovary.
- Development of the uterus divides gubernaculum into: ovarian ligament and round ligament.

II. Unequal growth of body of the fetus.

Number of ova:

- At 20 weeks → 2-5 millions.
- At birth → One million.
- At puberty → 300,000.

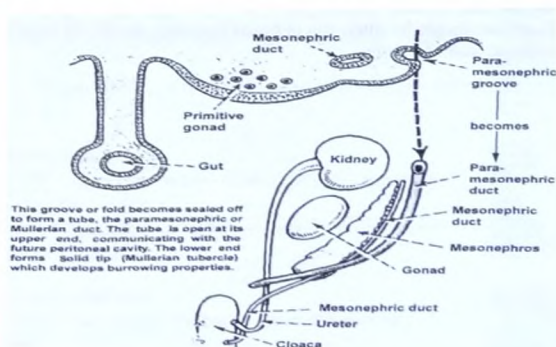


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- First meiotic division of germ cells starts at 8-12 weeks and become arrested at prophase (now, it is called 1ry oocyte).
- 1st meiotic division is completed after puberty just before ovulation (2ry oocyte + 1st polar body) and enters 2nd meiotic division and becomes arrested at metaphase.
- 2nd meiotic division is completed at time of fertilization (mature ovum + 2nd polar body).

Development of tubes, uterus and vagina :

- A longitudinal groove from coelomic epithelium on each side lateral to mesonephric duct called **Muller's groove**.
 - This groove deepens to form **Mullerian duct "paramesonephric duct"**.
 - The cranial end of Mullerian duct remains open and connected to coelomic cavity (peritoneal cavity).
 - The caudal end grows medially ventral to mesonephric duct to meet its fellow from opposite side.
 - Then, they pass side by side to reach back of definitive uro-genital sinus.
 - Now, Mullerian duct has 3 parts:
 - 1- Cranial → Vertical.
 - 2- Middle → Horizontal.
 - 3- Caudal → Vertical.
- The 2-caudal vertical parts fuse to form a single canal called uterovaginal canal, that pushes definitive urogenital sinus to produce **Muller's tubercle**.
 - The paramesonephric ducts modify to form the female genital duct.



Uterine tube:

It arises from the cranial vertical part of Mullerian duct. Its cranial end remains communicating with peritoneal cavity.

Uterus and cervix:

They arise from middle horizontal part of 2 paramesonephric ducts and cranial part of the uterovaginal canal.

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Vagina :

- 1- *Upper 4/5th* from the caudal part of the uterovaginal canal (mesodermal).
- 2- *Lower 1/5th* from the definitive urogenital sinus (endodermal).
- 3- *The septum in between* (Muller's tubercle) forms the hymen (later on an opening develops through it). Canalization of vaginal plate occurs at 18 weeks.

Development of the vulva :

- It starts at 7th week of gestation.
- Two folds will develop on each side of urogenital membrane:
 - Inner one → Urethral fold
 - Outer one → Genital fold
- The two genital folds fuse anteriorly to form genital tubercle. Then, differentiation will occur:
 1. **Genital tubercle** → Clitoris.
 2. **Two urethral folds** → Labia minora.
 3. **Two genital folds** → Labia majora.
 4. **Vestibule** is formed from urogenital sinus.
 5. **Urethra** is formed from urogenital sinus.
 6. **Bartholin gland** develops as an outgrowth from urogenital sinus.

Wolffian system in female :

It will undergo atrophy and form embryonic remnants between the two layers of the broad ligaments. These are:

- 1- **Kobelt tubules** which are found in the outer part of the broad ligament.
- 2- **Epoophoron**: Few tubules lying between the ovary and the tube.
- 3- **Paroophoron**: Tubules lying between the ovary and the uterus.
- 4- **Gartner or Wolffian (mesonephric) duct**: run in broad ligament parallel to tube, then to uterus, then in the antero-lateral wall of vagina.

Congenital anomalies of the female genital tract

Uterus, müllerian duct abnormalitis :

Congenital anomalies result from either:

- Defective organogenesis.
- Defective fusion.
- Defective septal resorption.

Müllerian duct anomalies are categorized most commonly into 7 classes according to the American Fertility Society (AFS) Classification Scheme as follows (1988):

I. Class I (hypoplasia/agenesis): Mayer-Rokitansky-Kuster-Hauser syndrome.

II. Class II (unicornuate uterus):

- A unicornuate uterus is the result of complete, or almost complete, arrest of development of 1 müllerian duct.
- This form may be associated with a rudimentary horn arising from the contralateral müllerian duct.



III. Class III (didelphys uterus):

- This anomaly results from complete nonfusion of both müllerian ducts.
- Didelphys uterus. Note the complete separation but full development of each müllerian duct



IV. Class IV (bicornuate uterus):

- A bicornuate uterus results from partial nonfusion of the müllerian ducts.
- The prominent fundal cleft (>1 cm) distinguishes the anomaly from septate uterus.



V. Class V (septate uterus):

- A septate uterus results from failure of resorption of the septum between the 2 uterine horns.
- The septum can be partial or complete, muscular or fibrous and can be of variable length.



VI. Class VI (arcuate uterus):

- An arcuate uterus has a single uterine cavity with a convex or flat uterine fundus.
- Arcuate uterus. Mild thickening of the midline fundal myometrium resulting in fundal cavity indentation but normal outer fundal contour.



VII. Class VII (diethylstilbestrol-related anomaly):

- Diethylstilbestrol (DES), an estrogen analogue prescribed to prevent miscarriage from 1945-1971.
- Female fetuses that are affected have a variety of abnormal findings that include uterine hypoplasia and a T-shaped uterine cavity, and adenosis of the vagina with



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increased risk of vaginal clear cell carcinoma. Imaging findings are pathognomonic for this anomaly.

- Diethylstilbestrol-exposed uterus. Myometrial hypertrophy results in a T-shaped uterine cavity and cavity irregularity, which is pathognomonic for the anomaly. Typically, the uteri are hypoplastic.

Disorders associated with congenital abnormalities of uterus:

- o Spasmodic dysmenorrhoea occurs with hypoplastic uterus.
- o Menorrhagia may occur with a bicornuate uterus due to increased surface area of endometrium.
- o Infertility because of uterine hypoplasia.
- o Ectopic pregnancy may occur in the rudimentary horn.
- o Abortion and preterm labour because of uterine hypoplasia, congenital weakness of uterine isthmus (incompetent cervix).
- o Malpresentation of the fetus as breech or transverse lie. Habitual Malpresentation suggests uterine malformation as bicornuate, septate and subseptate uterus.
- o Uterine inertia during labour due to uterine hypoplasia.
- o Labour may be obstructed by the nonpregnant horn of a bicornuate uterus or by a longitudinal vaginal septum.
- o Placenta accreta when the placenta implanted on uterine septum.

Congenital abnormalities of the ovaries:

- Aplasia or complete absence.
- Ovarian (gonadal) dysgenesis in the form of fibrous bands with no follicles "streak gonads" as seen in Turner syndrome.
- Accessory ovaries.
- Failure of descent into the pelvis.
- Ovotestis which is combined ovarian and testicular tissues seen in the true hermaphrodite.

Congenital abnormalities of the tubes:

- Aplasia.
 - Hypoplasia: the tube is long, narrow and tortuous.
 - Accessory ostia.
 - Congenital diverticulae.
- These anomalies predispose to tubal pregnancy.

Congenital abnormalities of the vagina:

- Aplasia. The vagina may be completely absent or is represented by a shallow depression (the part developing from the urogenital sinus).
- Hypoplasia. The vagina is short and narrow.
- Transverse or longitudinal septum.
- Congenital stricture.
- Double vagina (uterus didelphys).
- Congenital ureterovaginal, vesicovaginal or rectovaginal fistula.

Congenital abnormalities of the vulva:

- Hypoplasia. Infantile vulva as in Turner syndrome.
- Cysts as congenital dermoid cyst which occurs only in the midline.
- Accessory nipple or breast. The breasts and vulva lie in the milk line which extends from the axilla to the vulva.
- Hypertrophy of the clitoris (clitoromegaly : clitoridal index $>35 \text{ mm}^2$) which is usually associated with other manifestations of virilism.
- Hypertrophy of one or both labia minora (dog-ear labia minora).
- Ambiguous external genitalia as in congenital adrenal hyperplasia.
- Double vulva. There is duplication of the genital tract, urethra, and bladder.

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Vaginal agenesis (Aplasia)

- Absence of the whole vagina.
- Absence of upper 4/5th of vagina (developed from Mullerian ducts).

Diagnosis:

- Symptoms: amenorrhea (1ry).
- Signs: Absent vagina.
- U/S: confirm presence or absence of uterus.
- IVP: exclude renal anomalies.
- Testosterone level exclude testicular feminization syndrome.
- Chromosomal analysis exclude testicular feminization syndrome.

Treatment:

- If uterus is present: immediate removal of obstruction to allow menstrual flow.
- If uterus is absent: creation of new vagina.

1- Frank non operative method:

- Repeated application of vaginal dilators for 20 minutes / day.
- Functional vagina will be obtained after 6wk.

2- McIndoe's operation:

A space is dissected between bladder & rectum.

Split-thickness skin graft is applied over a mould then inserted into the pouch.

The mould is removed after 2-3 week.

After that the patient is given a new mould which is used until she starts intercourse. (The best dilator is the husband penis).

3- William's operation:

- U-shaped incision is done over vulva & perineum.

The inner edges are at first sutured together in the midline then the outer edges are sutured to make a tube for intercourse.

Imperforate hymen

It is due to failure of canalization of Mullerian duct.

Pathogenesis & pathology:

After puberty:

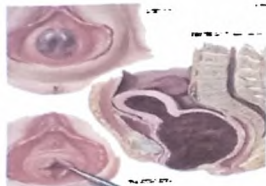
- Blood accumulate inside vagina causing distension → haematocolpos.
- Then haematometra → haematosalpinx.
- In neglected cases blood pass to peritoneal cavity causing adhesions.
- Some blood is absorbed so → blood is viscid dark brown.

Symptoms:

- 1ry amenorrhea.
- Cyclic lower abdominal pain.
- Abdominal swelling.
- Urinary symptoms: dysuria, acute urine retention or difficulty in micturition due to compression of urethra by vagina.

Signs:

- Generally: → 2ry sexual characters are well developed.
- Abdominally: Pelvi-abdominal mass tense cystic limited mobility (haematocolpos) with firm mass above (uterus).
- Vaginally: bulging bluish hymen.
- P/R: cystic mass in front of rectum.



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Investigations:

- U/S: → haematometra, haematocolpos.

Treatment:

- Under general anesthesia.
- Complete aseptic conditions.
 - Hymenotomy → Cruciate incision (by diathermy) + trimming of edges.
 - Allow slow escape of blood.
 - Prostaglandins may be of value in some cases.
- Antibiotics to prevent infection:
 - Blood a good medium of infection.
 - Absence of lactobacilli.
- A certificate should be given to the patient.

Physiology of menstruation

Ovarian cycle

- It starts after puberty.
- The ovary undergoes cyclic changes which is responsible for all changes occurring in genital tract.
- It passes in the following stages:

(A) Follicular phase :

1- Primordial follicles : is made of :

→ oocyte arrested in prophase of 1st meiotic division.

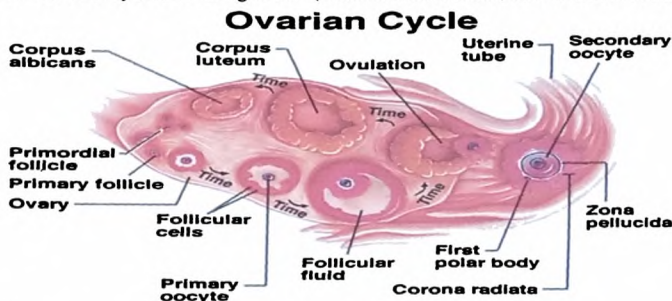
→ Single layer of flat cells "granulosa cells".

2- Spontaneous growth of a number of follicles >100 occur, the mechanism of initial growth is unknown → "not dependant on FSH and LH". This process occurs 3 cycles prior to ovulation (Recruitment)

- The 1st sign of growth is granulosa cells become cuboidal and form multiple layers around oocyte.

3- Pre-antral follicle :

- The oocyte expands and become surrounded by "Glycoprotein coat around oocyte, hyaline membrane" → **Zona pellucida**.
- Fluid filled spaces appear between granulosa cells.
- Granulosa cells synthesis estrogen "E2" (from androstenedione) and inhibin hormone.



Selection and dominance :

- Only one follicle will continue growth while the others undergo atresia by the 6th day due to:
 - The follicle that will become dominant contains highest number of FSH receptors.
 - Increasing level of E2 and inhibin → -ve feedback on FSH production by pituitary → relative ↓ FSH.
 - Other follicles cannot convert androstenedione to E2 → accumulation of androstenedione in these follicles → atresia "atretic follicles".
 - Dominant follicle will not be affected because it very sensitive to FSH and will escape atresia.
 - Inhibin is involved in the process of atresia of other follicles.
- 4- Antral follicle :
 - The fluid filled spaces will coalesce and form one fluid filled space pushing oocyte with its surrounding cells to one side.
 - Cells surrounding oocyte are called corona radiata and cumulus oophorus.
 - Ovarian stroma around growing follicle differentiate into:

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→ Theca interna :

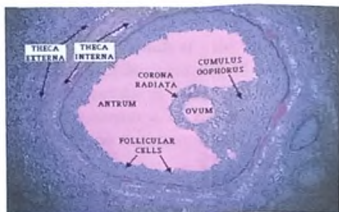
- Large cells produce steroids.
- Highly vascular.

→ Theca externa :

- Flat theca cells.
- Less vascular.

Now it is called **mature Graffian follicle** "18-24mm" *which consists of :*

- 1- Ovum "120 μ m in diameter".
- 2- Perivitelline space.
- 3- Zona pellucida.
- 4- Corona radiata.
- 5- Cumulus oophorus.
- 6- Granulosa cells and antrum containing fluid.
- 7- Theca interna cells.
- 8- Theca externa cells.



(B) Ovulation :

- 1- It is extrusion of ovum with the surrounding layer of granulosa cells "corona radiata" from Graffian follicle into peritoneal cavity.
- 2- It occurs 36h from onset of LH surge and 12 h after Peak of LH surge.
- 3- LH surge stimulates:
 - Completion of 1st meiotic division (1st polar body + 2ry oocyte).
 - Luteinization of granulosa cells.
 - Formation and maintenance of corpus luteum.
 - Synthesis of progesterone and prostaglandins.

Mechanism of ovulation :

- \uparrow proteolytic activity " \uparrow proteases, collagenase".
- PG $\rightarrow \uparrow$ contraction of smooth muscles around Graffian follicle $\rightarrow \uparrow$ intrafollicular pressure.
- PG $\rightarrow \uparrow$ follicular fluid $\rightarrow \uparrow$ intrafollicular pressure.
- Progesterone released from luteinized cells $\rightarrow \uparrow$ FSH surge "smaller than LH surge" \rightarrow will aid process of ovulation.

(C) Luteal phase :

- 1- Granulosa \xrightarrow{LH} lutein cells. - Theca cells \xrightarrow{LH} para lutein cells.
- 2- The follicle after ovulation is transformed into corpus luteum which is:
 - More vascular.
 - High content of "cholesterol and carotin" \rightarrow yellow in color.
 - Granulosa cells and theca cells proliferate and produce progesterone mainly and estrogen.
- 3- Fate:
 - \uparrow progesterone \rightarrow -ve feedback on LH release \rightarrow degeneration of corpus luteum \rightarrow corpus albicans $\rightarrow \downarrow$ P and E level \rightarrow menstruation.
 - Usually corpus luteum survives for 14 days.
- 4- If pregnancy occurs: Growing ovum \rightarrow HCG \rightarrow maintenance of corpus luteum \rightarrow corpus luteum of pregnancy.

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Hormonal control of ovarian cycle

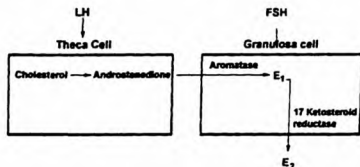
- Hypothalamus produces "**GnRH**" (gonadotrophin releasing hormone "**pulsatile manner**"):
 - Pulse frequency in 1st half of cycle "follicular phase" is every 60- 90 min.
 - Pulse frequency in 2nd half of cycle "luteal phase" is every 120- 180 min.
- These will reach pituitary via hypothalmo-hypophyseal portal circulation.
- Basophil cells of pituitary will release → FSH and LH "follicle stimulating hormone" and "luteinizing hormone".

Hypothalamus is under control of :

- Cerebral cortex. → Emotions.
- Diet. → Feedback mechanism "sex hormones".

During follicular phase :

- Initial growth of follicles is not dependent on gonadotrophins while if not followed by stimulation by FSH, atresia will occur.
- Low level of estrogen in the blood at the beginning of cycle stimulate pituitary to produce FSH and to lesser extent LH.
- FSH → stimulates growth of follicles.
- Two cell theory of steroidogenesis.
- ↑ Estrogen production from the follicle:



will lead to:

- Increased FSH and LH synthesis but ↓ secretion → drop in FSH level → atresia of all follicles except the dominant follicle "contain ↑ FSH receptors".
- Also ↑ inhibit will aid this process by inhibition of pituitary FSH not GnRh.
- Synthesis of LH receptors on granulosa cells of the dominant follicle.
- At midcycle:** when E2 level is sustained (48-50 hr) above a critical level (>200 pg/ml), it will lead to increase in amplitude and frequency of GnRh pulses which exert a positive feedback on LH → **LH surge**.
- Midcycle increase in progesterone is essential to ensure sufficient LH receptors amount.

LH surge :

- Stimulate completion of 1st meiotic division and oocyte will enter 2nd meiotic division and arrest at metaphase.
- Causes luteinization of granulosa cells → preovulatory release of small amount of progesterone.
 - This progesterone :
 - facilitates the feed back of E2 on LH.
 - causes small FSH surge.
 - FSH surge :
 - Causes important intrafollicular changes necessary for ovulation.
 - Causes production of LH receptors in sufficient number on granulosa cells.
- Stimulates synthesis of PGE2 and F2 before ovulation.
- Post-ovulatory maintenance of corpus luteum.
 - Mechanism of ovulation: → "see ovulation".

Luteal phase :

Corpus luteum produces progesterone and E2 under effect of LH:

- If pregnancy does not occur:
 - ↑ level of progesterone and estrogen will cause -ve feedback on hypothalamus → ↓ GnRH → ↓ LH → degeneration of corpus luteum → corpus albicans.

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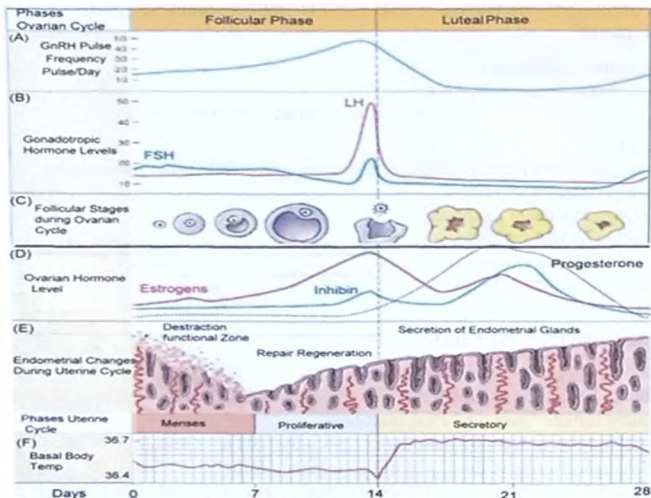
This will result in ↓ E and P level in the blood :

→ menstruation.

→ release of pituitary from -ve feedback inhibition and new cycle will start “↑FSH”.

• If pregnancy occurs:

- Growing ovum → ↑ HCG “similar to LH” → maintains corpus luteum function till 10- 12 wk when the placenta will be formed.



Menstrual cycle

Menstruation:

- Cycle uterine bleeding caused by shedding of progestational (secretory) endometrium.
- It occurs between menarche (1st menstruation) and menopause (cessation of menstruation).
- It includes shedding of superficial and middle layer of endometrium leaving basal layer.

Characteristics of menstruation:

- 1- Menarche : It is the 1st menstruation in female life “10- 16 years” - 13 years in average.
- 2- Duration of bleeding: **2- 7 days**
 - If > 7 days → menorrhagia.
 - If < 2 days → hypomenorrhea.
- 3- Amount : **20- 80 ml**
 - If > 80 ml → menorrhagia.
 - If > 20 ml → hypomenorrhea
 - Usually females change 3 napkins/ day (2/day and 1/ night).
- 4- Length of cycle : **3- 5 weeks**, average 4 weeks → 28 days.
 - < 3 wk → polymenorrhea.
 - > 5 wk → oligomenorrhea.
- 5- Menstrual blood does not coagulate : at first coagulates in the uterine cavity but rapidly liquefies by fibrinolysins (plasmin) secreted by endometrium → so menstrual blood is devoided of fibrinogen.
 - Blood will coagulate if : → severe bleeding or ↓ fibrinolysins.

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6- Menstrual discharge consists of :

- Blood.
- Mucous "cervical".
- Leucocytes.
- Endometrial fragments.
- Enzymes and prostaglandins.

7- Menstrual molimina : Mild symptoms occur 7- 10 days before menstruation which is relieved once menstruation occur.

- The symptoms include heaviness of the breasts, nausea, irritability or depression.
- If these symptoms are exaggerated → premenstrual syndrome (PMS)

• Mechanism of menstruation :

- Degeneration of corpus luteum → ↓ E and P level → ↓ edema and shrinkage of endometrium → more coiling of spiral arterials → ischemia and necrosis of superficial and middle layer of endometrium.
- Necrotic area separates → bleeding.
- The exact mechanism of menstruation is not understood.

• Control of bleeding :

- The degenerated endometrium → prostaglandins:
 - PG F2 alpha → uterine contraction + V.C.
 - Thromboxan A2 → V.C. + platelet aggregation.
- Regeneration of endometrium from basal layer.

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Cyclic changes of endometrium

| | (1) Proliferative phase | (2) Secretory phase |
|-----------------------|--|---|
| Duration | 9- 11 days - Starts after the end of menstruation. - Ends at time of ovulation. | 14 days (constant): - Starts with ovulation. - Ends with onset of menstruation. |
| Hormonal control | - Estrogen released from mature graffian follicle. - It will stimulate growth and proliferation of endometrium from basal cell layer. - It passes through 2 days of resting stage. | - <u>Progesterone</u> released from corpus luteum. - It produces secretory changes in estrogen primed endometrium. |
| Endometrial thickness | 3-4 mm | 6-8mm |
| Glands | ↑ number and length <u>tubular</u> and <u>no secretion</u> | ↑ length and become <u>tortuous</u> "cork screw" or saw-tooth appearance" - filled with <u>secretions</u> "glycogen and mucin" |
| Epithelium | Low columnar | - high columnar with: - sub nuclear vacuoles. - supra nuclear vacuoles. |
| Stromal cells | ↑ in size and become globular. | -↑ in size and become polygonal -↑ cytoplasm. |
| Stroma | Dense and formed of single layer. | - Edematous and PNL infiltration occur "3 days before menstruation". - Endometrium is differentiated into 3 layer: 1) <u>Superficial compact layer</u> : around necks of glands. Cells closely packed together. 2) <u>Middle spongy layer</u> : around distended lumen of glands. 3) <u>Deep basal layer</u> : around basal part of glands. |
| Vascularity | Gradually increased | ↑ greatly and 2 types of arterioles: 1) <u>Basal arterioles</u> : short, straight anastomose freely to supply basal layers. 2) <u>Spiral arterioles</u> : spiral and supply superficial layer and don't anastomose (end arteries). |

I. Basic Gynecology

Cyclic changes of cervical mucus

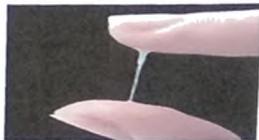
| 1 st half of the cycle | 2 nd half of the cycle |
|--|--|
| <ul style="list-style-type: none">* Estrogenic effect :<ul style="list-style-type: none">- Excessive.- Watery.- Acellular.* +ve Spinbarrkiet test →* Contains NaCl, KCl* +ve Fern test* Parallel mucous threads. | <ul style="list-style-type: none">* Progesterone effect.<ul style="list-style-type: none">- Scanty.- Viscid.- Contains leucocytes.* -ve Spinbarrkiet test.* does not contain NaCl, KCl.* -ve Fern test.* Cross linked mucous thands. |

→ Estrogenic effect is maximums 24- 36h before ovulation.

- Spinbarrkiet test "Thread test":

A drop of mucous on tip of artery forceps and the artery is opened →

- Cervical mucous become down into thread.
- Can be done using 2 slides.



- Fern test:

Adrop of mucous is left to d;ry on a slide and examined by microscopy

- → arborization "NaCl/ KCl crystals"
- → palm leaf appearance.



Cyclic changes of vaginal epithelium

- Vaginal epithelium: non-keratinized stratified squamous epithelium.
- Desquamation occurs continuously

| 1 st half of cycle | 2 nd half of cycle |
|--|--|
| <p>"Estrogen effect"</p> <ul style="list-style-type: none">• E → maturation of epithelium and shedding of <u>superficial cells in vaginal smear</u> :<ol style="list-style-type: none">1. Separate.2. Eosinophilic cytoplasm.3. Pyknotic nucleus.4. Clear background "few leukocytes" | <p>Progesterone effect</p> <ul style="list-style-type: none">• P → causes shedding of <u>intermediate cells in vaginal smear</u> :<ol style="list-style-type: none">1. Clumped together.2. Basophilic cytoplasm.3. Vesicular nucleus.4. Background contains many leukocytes.5. Navicular cells "folded border" |

Maturation index :

Parabasal/ intermediate/ superficial cells.

II. Reproductive endocrinology and infertility

Reproductive endocrinology and infertility

Amenorrhea

Definitions:

Absence or cessation of menstruation (it is a symptom not a disease)

1ry amenorrhea

- Absence of menstruation till age of 16y in presence of 2ry sex characters.
- Absence of menstruation till age of 14y in absence of 2ry sex characters.

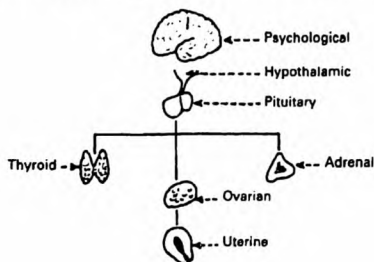
2ry amenorrhea

- Absence of menstruation for 3 cycles "if it was previously regular".
- Absence of menstruation for 6m "if it was irregular".

Classification:

(1) Physiological:

- 1- Before puberty: low GnRH level.
 - 2- After menopause: all follicles are used up.
 - 3- Pregnancy: commonest cause of 2ry amenorrhea.
 - High level of E & P \rightarrow \downarrow gonadotrophins.
 - 4- Lactation: prolactine hormone
 \rightarrow \downarrow production of GnRH.
 \rightarrow makes ovary refractory to gonadotrophins.
 \rightarrow \downarrow ovarian steroidogenesis.
 - 5- Short periods after puberty: due to immaturity of hypothalamo- pituitary- ovarian axis.
- Short periods before menopause: (\downarrow number of follicles- \uparrow resistance to gonadotrophins).



(2) Pathological:

- **False amenorrhea (cryptomenorrhea):**
Menstruation occurs but blood is unable to escape from genital tract due to obstruction of outflow tract.
- I. **1ry amenorrhea (congenital causes):**
- 1- Imperforate hymen (commonest causes) See Before.
 - 2- Complete transverse vaginal septum.
 - 3- Vaginal aplasia.
 - 4- Cervical atresia (congenital)

II. Reproductive endocrinology and infertility

II. 2ry amenorrhea (acquired causes):

- 1-Post operative vaginal adhesions (vaginal gynatresia) after difficult instrumental delivery.
- 2- Cervical amputation, excessive cauterization or conization.

▪ True amenorrhea:

1- **Compartment I:** Uterine (end organ) causes.

2- **Compartment II:** Ovarian causes.

3- **Compartment III:** Pituitary causes.

4- **Compartment IV:** Hypothalamic causes.

5- **General causes:** Endocrinal and non-endocrinal.

Compartment I: Uterine amenorrhea

1. Congenital aplasia (Mullarian agenesis = Mayer-Rokitansky-Kuster-Hauser syndrome):

- Genotype: 46XX (normal female).
- Primary sex organ: normal ovary with normal follicles.
- Hormones: normal estrogen and progesterone.
- Defect: lack of Mullarian duct development:
 - Uterus absent or rudimentary.
 - Tubes absent or rudimentary.
 - Vagina is absent or presented by small pouch (developed from urogenital sinus).
- Association: Renal (30%) & skeletal anomalies (15%).
- Secondary sex character: normal female secondary sex character.

2. Uterine hypoplasia (rudimentary or infantile uterus).

3. Androgen insensitivity "testicular feminization syndrome": (Morris syndrome)

Etiology: inherited → x linked recessive.

Pathogenesis:

- Genotype → 46XY → gonads testis.
- Testis:
 - Sertoli cells → anti-mullerian hormone → inhibit development of mullerian ducts (tube, uterus, upper vagina).
 - Interstitial cell of leyding: testosterone (male level).
 - Target organs: **(No androgen receptor)**
 - external genital → develop as a female.
peripheral conversion
- Testosterone $\xrightarrow{\text{peripheral conversion}}$ Estrogen → female characteristics.



Clinical picture: Attractive female

- Gonads:
 - Testis: - No spermatogenesis.
 - Secretes androgen (male level).
 - Found in inguinal canal, hernial sac, upper labia.
- Genital organs:
 - Uterus, tubes, upper vagina → absent.
 - Lower 1/5 of vagina → developed from uro-genital sinus
 - → short blind vagina.
 - Vulva → normal.
- Breast:
 - well developed, large, hemispherical, smooth contour,
 - small under developed nipple & pinkish pale areola.

II. Reproductive endocrinology and infertility

- Smooth hairless skin.
- Scanty- absent pubic hair.

Types:

- 1- Complete (most common).
- 2- Incomplete (less common):
Female features + variable degree of virilism.

Investigations:

- 1- Androgen level (7.8ng/ ml).
- 2- Laparoscopy & biopsy (testis).
- 3- Buccal smears → no bar body.
- 4- Chromosomal pattern 46XY.

D.D:

| | Testicular feminization | Mullerian agenesis |
|-----------------------------------|-------------------------|--------------------|
| Genotype. | 46 XY | 46 XX |
| Gonads. | Testis | Ovaries |
| Androgen level. | Male level | Female level |
| Pubic & axillary hair. | Abscent | Normal |

Treatment:

- Removal of testis (risk of malignancy 2- 25%) after puberty 16- 18y (Because developmental changes achieved with exogenous hormones do not seem to match the smooth pubertal changes due to endogenous hormones).
- Estrogen is given to avoid (menopausal symptoms- osteoporosis).
- Plastic surgery to convert vaginal pouch into functioning vagina.
- 4. Surgical removal (hysterectomy).
- 5. Destruction of basal layer of endometrium by T.B. or radiotherapy.
- 6. Refractory endometrium (lack of steroid receptors).
- 7. Asherman's syndrome (intra uterine adhesions):

Etiology:

- 1- Excessive uterine curettage: after abortion, post-partum, diagnostic or therapeutic.
2. Uterine infection: post abortive, post- partum .
3. Myomectomy (if the cavity is opened) & C.S.
4. T.B. endometritis (**Netter syndrome**).

Degrees: → by Hysteroscopy.

- Minimal: < ¼ uterine cavity.
- Moderate: ¼- ¾ uterine cavity.
- Sever: > ¾ uterine cavity.

Clinical picture:

- History of operation or infection.
- Symptoms:
 - 1- Hypomenorrhea- amenorrhea.
 - 2- Dysmenorrhea.
 - 3- Infertility.
 - 4- With pregnancy:
 - Recurrent abortion.
 - Recurrent preterm labor.
 - Placenta previa.
 - Placenta accreta.

II. Reproductive endocrinology and infertility

- Signs:
 - Failure of sound passage.
 - Failure of E & P withdrawal bleeding.
- Investigation:
 - Hysteroscopy (most accurate).
 - HSG → filling defect.
 - Sonohysterography.
 - TVS: may help in detection of islands of normal endometrium

Treatment:

- 1- Lysis of adhesions using resectoscope → hysteroscopic guided.
- 2- Keep uterine wall apart (large IUD "lippes loop" or ballon catheter).
- + Anti-adhesion: corticosteroids. + Prevent infection → antibiotics.
- 3- Cyclic estrogen & progesterone → 3 month "high dose" → proliferation of endometrium.

Compartment II: Ovarian amenorrhea

1- Ovarian hypofunction:

1. Gonadal dysgenesis (Turner syndrome). See below
2. Premature ovarian failure or insufficiency → see premature menopause.
 - It occurs before the age of 40 due to autoimmune disease, ovarian destruction by chemo or radiotherapy: there is no primordial follicles low Estrogen and Progesterone high FSH and secondary Amenorrhea.
3. Resistant ovary syndrome (Savage syndrome):
Ovaries contain follicles but fail to respond to Gn (FSH & LH) due to ↓ receptors or ↓ sensitivity → Amenorrhea & infertility.

*** Investigations:**

- E₂ ↓.
- ↑ FSH (> 25mlu/ ml) & ↑ LH.
- Ovarian biopsy → ovary contains ovarian follicles.

*** Treatment:**

- 1- Cyclic E & progesterone → may be followed by spontaneous recovery.
- 2- Large doses of gonadotrophins for → induction of ovulation.
- 3- Ovum donation → condemned in Islam.
4. Surgical removal of ovary.
5. Destruction of ovary by malignancy, radium or T.B.

N.B: * Spontaneous recovery may occur.

2- Ovarian hyperfunction:

1. Polycystic ovarian syndrome.
2. Theca-granulosa cell tumour (high estrogen).
3. Virilizing ovarian tumours:

Androblastoma, lipoid cell tumours.

→ Defeminization → virilization

Treatment: surgical removal.

II. Reproductive endocrinology and infertility

Turner syndrome

Definition: Chromosomal anomaly (45 XO patient) in which the ovaries are dysgenetic or streak and formed only of undifferentiated stroma.

Genotype:

- Classic Turner: 45 XO.
- Mosaic turner: 45XO / 46XX
- Incomplete Turner:

- Deletion on short arm of X chromosome → short stature & physical abnormalities of turner.
- Deletion on long arm of X chromosome → streak gonads.

N.B. Mixed gonadal dysgenesis: 45XO/ 46XY (high risk of development of gonadoblastom, so they should be removed).

Phenotype:

- Ovaries: **Streak gonads** (undifferentiated stroma - no follicles).
- 1ry amenorrhea (hypergonadotrophic hypogonadism).
- Genital organs: infantile uterus & vagina.
- Lack of secondary sexual characters.
- Physical characteristics:
 - short stature.
 - webbing of neck.
 - Widely spaced nipple & under developed breast.
 - Coarctation of aorta. Cubitus valgus.
 - Abnormalities of fingers & toes.
- ↑ incidence DM, HPN, color blindness.



N.B.: Cases of **mosaic turner** → has small number of ova → menstruate, can conceive but will have premature ovarian failure.

Investigations:

- 1- FSH > 40 mIU/ml - E2 → low.
- 2- X-ray → retarded bone age.
- 3- Laparoscopy → streak gonads.
- 4- Karyotyping → 45 XO.
- 5- Buccal smear → absent Barr body.

Treatment:

(1) Cyclic estrogen & progesterone:

E → development of 2ry sex characters and prevent osteoporosis.

P → to prevent endometrial carcinoma.

Treatment started **after 13 years old** to prevent premature closure epiphysis → short stature.

(2) Cases with mosaic pattern XO/ XX → premature ovarian failure → HRT.

N.B.: Cases with mixed gonadal dysgenesis XO/ XY → premalignant 25% → surgical removal of gonads + HRT.

II. Reproductive endocrinology and infertility

Compartment III: Pituitary amenorrhea

1. Pituitary infantilism: (Levi- Lorain syndrome)

- ↓ GH → short stature (dwarfism).
- ↓ Gonadotrophins → hypogonadism (infantilism) & 1ry amenorrhea.

2. Panhypopituitarism: (Pituitary cachexia) Sheehan's syndrome:

Definition: Pan anterior hypopituitarism (of variable degree) in a female due to obstetric hemorrhage.

Etiology: It is due to ischemic necrosis of ant. Pituitary due to spasm & thrombosis of arteries due to post-partum hemorrhage & shock.

Types:

1- Complete type: 95 % of anterior pituitary gland is destroyed (*all* anterior pituitary gland hormones are decreased).

2- Incomplete type: when ≥ 75 % of anterior pituitary gland is destroyed (only *some* anterior pituitary gland hormones are decreased).

Clinical picture:

- History of sever postpartum (occasionally antepartum).
- Failure of lactation "1st clinical sign" (↓ prolactin).
- 2ry amenorrhea & genital atrophy (↓ FSH & LH).
- Hypothyroidism (↓ TSH):
 - Apathy.
 - ↓ HR.
 - Intolerance to cold & constipation.
- Adrenocortical insufficiency (↓ ACTH):
 - Loss of pubic & axillary hair.
 - hypotension, hypoglycemia & wt loss.
- ↓ Pigmentation (↓ MSH).

Investigations: Hormonal assay (decrease level of ant. pituitary hormones).

Differential diagnosis:

Causes of **postpartum amenorrhea** (postpartum period is usually six weeks, in special circumstances is extended to six months following delivery):

1- Causes related to pregnancy:

- | | |
|--------------------------|------------------------|
| a) Lactation. | b) New pregnancy. |
| c) Sheehan syndrome. | d) Asherman syndrome. |
| e) Hysterectomy. | f) Vaginal gynatresia. |
| g) Postpartum psychosis. | |

2- Any cause for secondary amenorrhea occurring after labor.

3- Mosaic Turner syndrome (46XX/45XO): She had menstruation and got pregnant but she has small number of follicle → premature menopause.

Treatment: "Replacement"

1. Corticosteroids then Thyroxin for life.
2. → If pregnancy is desired → induction of ovulation (HMG; FSH & LH).
→ If pregnancy is not desired → cyclic E & P.

Simmond's disease:

- Due to any cause other than obstetric hemorrhage (destruction of ant. lobe of pituitary).
- Affects both sexes.
- The same C/P of Sheehan's syndrome

II. Reproductive endocrinology and infertility

3. Pituitary adenoma:

Prolactinoma (↑ prolactine)

Chromophobe adenoma:

- destruction of rest of gland → amenorrhea.
- optic atrophy, diagnosed by X-ray.

Acidophil adenoma: ↑ GH (gigantism - acromegally) + amenorrhea.

Basophil adenoma: ↑ ACTH → (Cushing disease):

- Amenorrhea.
- Trunkal obesity.
- Hirsutism.
- Stria.
- Tendency to develop (HPN- DM).

Prolactinomas

- It causes: Amenorrhea + Galactorrhea
- Macroadenoma > 1cm (common in male)
- Microadenoma < 1cm (common in female).

Incidence:

- Prolactinoma is the most common type of pituitary tumours (30% of all pituitary adenomas), and may occur as part of inherited condition (multiple endocrine neoplasia type1).
- More common in females than males (5 times) & rare in children.

All the macroadenomas lead to:

- Hormonal disturbances .
- Pressure on the optic tract & chiasma (visual disturbances).
- Features of a raised intra-cranial tension (severe persistent headache)
- Widening of the pituitary fossa (diagnosed by CT).

Treatment:

- Medical treatment should be tried first (dopaminergic agonists).
- Hypophysectomy either trans-cranial or trans-nasal (trans-sphenoid).

4. Empty sella syndrome:

Etiology: leakage of C.S.F through diaphragma sellae (herniation of subarachnoid space) → pressure atrophy on pituitary gland.

Clinical picture:

- There is amenorrhea (↓ GnH) + galactorrhea (↓ dopamine → ↑ prolactine).
 - Adrenal & thyroid are usually not affected.

Diagnosed by CT.

Treatment: Hormone replacement or induction of ovulation.

5. Craniopharyngioma: → It may cause pressure atrophy on gonadotrophine secreting cell.

Compartment IV: Hypothalamic amenorrhea

Any disturbance of hypothalamus could affect GnRH leading to amenorrhea.

1. Organic lesion:

- Traumatic: fracture base of skull.
- Inflammatory: meningitis, encephalitis.

II. Reproductive endocrinology and infertility

5. Drugs:

1- Post- pill amenorrhea (Shearman's syndrome): < 1%

- (Pills → ↓ GnRH → ↓ FSH & LH → inhibit ovulation).
- Occasionally amenorrhea persists after stoppage of pills.
- It usually resolves spontaneously within 6 months.
- If it persists > 6m "investigate as a case of 2ry amenorrhea".

N.B.: depoprovera produces amenorrhea on long term use (atrophic endometrium).

2- Phenothiazine derivatives as reserpine & alpha methyl dopa → ↓ release of dopamine →

↑ prolactine level.

* Treatment:

- Treatment of the causes.
- If no cause was found → GnRH in pulsatile manner "by special pump".
- In post pill amenorrhea we may give → clomiphene citrate.

Other endocrinal causes of amenorrhea

1. Thyroid disorder:

* Hyperthyroidism: usually cause amenorrhea but can cause menorrhagia at first.

* Hypothyroidism: usually cause menorrhagia but can cause amenorrhea and galactorrhea.

2. Supra-renal disorder:

(A) Addison's disease: general debility, amenorrhea, hypotension, low cortisol level.

(B) Cushing syndrome: excess cortisol, androgen → moon face, buffalo hump, truncal obesity hirsutism, stria, DM, HPN, amenorrhea.

(C) Congenital adrenal hyperplasia.

3. Uncontrolled DM (obesity, nutritional disturbance & emotional)..

General causes of amenorrhea

1. Malnutrition (starvation & malabsorption).

2. Marked obesity (BMI >30) is usually associated with Hyperinsulinemia, metabolic and hormonal disturbances.

3. Acute illness may be followed by short period of amenorrhea.

4. Chronic illness: severe anemia, T.B., chronic nephritis.

5. Overwork, stress and exhaustion: prolonged work, physical stress or psychic stress about the study and exam may alter the higher centers.

Chromosomal causes

1- Turner syndrome. See before.

2- Super female: 47XXX or 48 XXXX

- 1ry amenorrhea, oligomenorrhea.

- Infertility.

- Infantile genital organs.

- Mental deficiency.

Diagnosis: Buccal smear → additional bar body.

Treatment: trial for induction of ovulation by Gonadotrophins → but may fail (refractory).

3- Androgen insensitivity "testicular feminization syndrome": (Morris syndrome)

II. Reproductive endocrinology and infertility

Causes of Amenorrhea

| | Causes of 1ry amenorrhea | Causes of 2ry amenorrhea |
|--|--|--|
| Pathogenesis | All congenital causes or acquired lesions appear before puberty | Any lesions or disease appear after puberty |
| (1) Physiological: | - Before puberty. | - Pregnancy. - Lactation. - Menopause. - Short periods (after puberty-before menopause). |
| (2) Pathological: | | |
| <u>A. False:</u> | - Imperforate hymen. - Complete transverse vaginal septum. - Vaginal aplasia. - Cervical atresia. | - Post-operative (cervical obstruction- vaginal obstruction). |
| <u>B. True:</u> | | |
| Uterine | - A plasia (mullerian agenesis). - Hypoplasia. - Refractory endometrium. | - Surgical removal. - T.B. - Asherman's syndrome |
| Ovarian | - Aplasia. - Turner syndrome. - Resistant ovary syndrome. | - PCO. - Surgical removal. - Destruction (TB, irradiation). - Functioning ovarian tumors. - Premature menopause. |
| Pituitary | - Levi- lorain. - Pituitary adenoma before puberty. Gigantism. - Empty sella syndrome. | - Simmond's disease. - Sheehan's syndrome. - Adenoma after puberty. |
| Hypothalamic | - All hypothalamic causes if before puberty. - Syndromes: all except Chiari-frommel & post-pill amenorrhea. | - All hypothalamic causes after puberty. |
| General & other endocrinal: | All causes before puberty: -Thyroid: cretinism -Adrenal: cong-adrenal hyperplasia. | All causes after puberty. |
| Chromosomal | - Testicular feminization syndrome. - Turner's syndrome. - Superfemale. | Mosaic turner (46XX/ 45XO) → premature ovarian failure. |

II. Reproductive endocrinology and infertility

Investigations of a case of amenorrhea

The investigations differ according to the type of amenorrhea either primary or secondary and the associated factors.

Primary amenorrhea

1) First, exclude:

- Cryptomenorrhea by inspection for imperforate hymen (developed secondary sex characters).
- Turner syndrome: physical characteristics, ↑FSH, ↓E2, absent Bar body & chromosomal analysis (45 XO).
- The rare androgen insensitivity syndrome: no internal genitalia by US, Buccal smear is negative (46 XY), masses may be felt in the inguinal region with hairless skin).

2) Hormonal assay:

- **FSH & LH:** Low (hypothalamic or pituitary defect), high (ovarian failure)
- **Prolactin:** If > 100 ng/ml: suggestion of adenoma.
- **Thyroxin** for thyroid lesions (low in cretinism).
- **TSH:** High in hypothyroidism.
- **Testosterone** (normal 0.2-0.8 ng/ml).
- **Growth hormone:** Low in pituitary infantilism.

3) Chromosomal studies:

- In Turner's disease, genetic make up is (45 XO)
- In androgen insensitivity syndrome (46XY).

4) Imaging techniques:

- **US** for the internal genital organs & ovaries.
- **CT & MRI** for the pituitary adenomas especially with high prolactin.
- **I.V.P** as uterine and vaginal malformations is often associated with congenital abnormalities in urinary system.

5) Endoscopy:

- Laparoscopy for the internal genitalia (hypoplasia, aplasia)
- Laparoscopy for the ovaries with biopsy (tumors, streak gonads, aplasia).

Secondary amenorrhea

1) First, exclude physiological amenorrhea as:

- (1) Pregnancy by US and pregnancy test.
- (2) Lactational: from history.
- (3) Menopausal: hot flashes, age, high FSH>25 mIU/ml.

NB: History of change of the environments of the patient, long standing illness, change in body weight and hair distribution must be noticed.

2) Then investigate by:

- (1) Hormonal assays as in primary amenorrhea.
- (2) CT & MRI if high prolactin is present.
- (3) Progesterone challenge test.
- (4) Hysteroscopy for Asherman syndrome.
- (5) Laparoscopy and ovarian biopsy for a premature ovarian failure.

II. Reproductive endocrinology and infertility

Step 1: Progesterone challenge test:

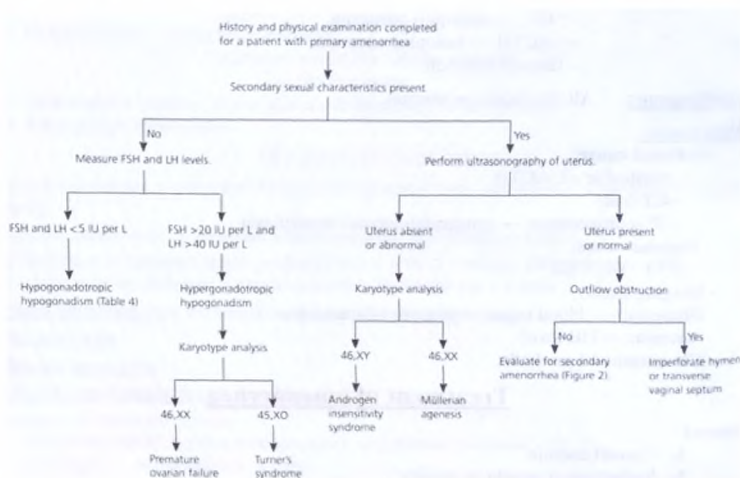
- * **Positive (withdrawal bleeding):** Anovulatory dysfunction, as the uterus has been primed by estrogen.
- * **Negative (no withdrawal bleeding):** There is deficiency of estrogen or lower genital tract defect.

Step 2: Cyclic Estrogen and progesterone:

- * **Negative (abnormal uterus):** Refractory endometrium for HSG and hysteroscopy.
- * **Positive (intact out flow tract):** Hypothalamic-pituitary ovarian defects.

Step 3: Measure FSH-LH:

- * **High:** Ovarian failure? Premature menopause.
- * **Low:** Hypothalamic-pituitary-defect.



1- Investigations of uterine amenorrhea:

- 1- Sound: cervical atresia, hypoplasia, Asherman.
- 2- HSG: asherman syndrome.
- 3- Hysteroscope: asherman syndrome.
- 4- Ultrasound: absent- hypoplastic uterus.
- 5- Laproscope: müllerian agenesis.
- 6- Endometrial biopsy: T.B.
- 7- Chromosomal: testicular feminization syndrom.

2- Investigations of ovarian amenorrhea:

- 1- U/S: PCO, ovarian tumors.
- 2- Laparoscope: streak gonads, PCO, tumor.
- 3- Hormonal assay – FSH > 40 mIU/ml → ovarian failure
– Turner's syndrome

II. Reproductive endocrinology and infertility

- Premature ovarian failure
- Surgical removal
- Resistant ovary syndrome.
- LH\ FSH \rightarrow 2:1 \rightarrow PCO
- 4- Chromosomal analysis
 - Turner (45XO)
 - Mosaic Turner (45XO/46XX) \rightarrow premature ovarian failure

3- Investigations of pituitary amenorrhea:

- 1- Visual field examination \rightarrow pituitary adenoma
- 2- Imaging (x-ray – CT-MRI)
- 3- Hormonal profile:
 - prolactin level
 - \downarrow all pituitary Hormones \rightarrow Sheehan syndrome.
 - \downarrow GH & gonadotrophins \rightarrow Levi-Lorain
 - \uparrow GH \rightarrow acidophil adenoma.
 - \uparrow ACTH \rightarrow basophil adenoma
 - Thyroid function.

4- Hypothalamic: All the above \rightarrow Normal.

5- Other causes:

- Adrenal cause:
 - cortisol level, ACTH
 - CT-MRI
 - 17 α progesteron \rightarrow congenital-adrenal hyperplasia
- Thyroid cause:
 - T3 , T4 , TSH
- Imaging (scan)
- Diabetes: \rightarrow blood sugar - glucose tolerance test
- Anemia: \rightarrow HB level.
- Chromosomal analysis.

Treatment of amenorrhea

1) General:

- 1- Correct anemia.
- 2- Reduction of weight in obesity.
- 3- Proper diet for the underweight.
- 4- Psychotherapy.

2) According to the cause:

- 1- Cruciate incision for the imperforate hymen.
- 2- Lyses of the intra-uterine adhesions by the resectoscope, then leave IUD and give exogenous estrogens.
- 3- Removal of any neoplasm (ovarian, pituitary or adrenal).
- 4- Bromocryptine for galactorrhea amenorrhea.
- 5- Thyroxin for hypothyroidism.

3) Induction of ovulation: In cases desiring pregnancy.

II. Reproductive endocrinology and infertility

4) Artificial menstruation:

- 1- Cyclic E & P Estrogen is given first, and then supplemented with Progesterone in last 10 days of cycle. in the hypo-estrogenic patients.
- 2- For normal or hyper estrogenic patients, give only progestogens (Provera 1x2x12 days from the 15th cycle day).
- 3- Contraceptive pills may be used.
- 4- Estrogens (ethinyl estradiol 50 micro or Premarin 1.25 mg daily for 21 days) in cases of atrophic endometrium as with DMPA amenorrhea.

Oligomenorrhea & hypomenorrhea

Oligomenorrhea: infrequent menstruation due to prolongation of cycle: > 35 days.

Hypomenorrhea: ↓ amount (<30 ml) &/or ↓ duration (<2days)

Commonly → oligo-hypomenorrhea (together)

Etiology:

- 1- Constitutional: dating since puberty
Patient → ovulating, fertile, normal
→ No treatment
- 2- Pathological: causes, investigations & treatment of amenorrhea.
- 3- May precede menopause.

Hyperprolactinemia

1. Prolactin hormone is polypeptide hormone secreted from lactotrophs (acidophils of anterior pituitary).
 2. Serum prolactin level: 5-20 ng/ml in non-pregnant non-lactating female.
 3. The discrepancy between serum prolactin levels and its clinical effects is due to presence of many isoforms with different biologic activities. Prolactin has 4 forms:
 - **Small prolactin** (low molecular weight and highest bioactivity).
 - **Big prolactin.**
 - **Big-big prolactin.**
 - **Glycosylated prolactin** (lowest bioactivity).
- Control of prolactin release:
- Prolactin inhibiting factor (dopamine) → ↓ prolactin release.
 - Estrogen → ↑ prolactin release.
 - TRH "thyrotropin releasing hormone" → ↑ prolactin release.

Hyperprolactinemia is the increase in the level of prolactin > 20 ng/ml (400mIU/ml) not related to pregnancy or lactation.

Galactorrhea is abnormal milk like secretion from breast of non-lactating female.

Causes of hyperprolactinaemia:

1- Physiological:

- Pregnancy (due to high E levels but no galactorrhea due to competition of E on prolactin receptors).
- Lactation.
- Stress.
- Sexual intercourse.
- Sleep
- Frequent nipple stimulation.

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2- Pharmacological:

- Estrogen containing drugs/ pills.
- Antidopaminergic drugs:
 - Tricyclic antidepressant (TCA).
 - Anti emetics → metoclopramide.
 - Antihypertensives: α methyl dopa and reserpine.

3- Pathological:

- Pituitary:
 - Pituitary adenoma "Prolactinoma".
 - Growth H. secreting tumor.
- Hypothalamic:
 - Decrease PIF (dopamine) secretion or access to pituitary.
 - Organic lesion: trauma, infection, tumors.
 - Psychological disturbance.
- Primary hypothyroidism:
 - Increase TRH → stimulates lactotrophs to ↑ prolactin secretion.
- Other causes:
 - Liver cell failure.
 - Chronic renal failure.
 - Chest wall disease
 - Ectopic secretion: "Paramalignant syndrome"
 - Hypernephroma of kidney.
 - Oat cell carcinoma of lung.
 - Hyperestrogenic states e.g PCOS.

4- Functional (idiopathic)

Clinical picture:

1- Galactorrhea: Only in 33 % of cases of hyperprolactinemia due to:

(A) Prolactin will not act in hypo or hyperestrogenic conditions.

(B) immunoactive prolactin may be non-bioactive.

2- Infertility: due to:

- Anovulation (group IV).
- Luteal phase defect.

3- Oligohypomenorrhea, even amenorrhea:

- Prolactin:
- ↓ pulsatile release of GnRH.
 - ↓ action of gonadotrophins on ovary.
 - ↓ ovarian steroidogenesis.

4- Rarely:

- Habitual abortion: due to luteal phase defect.
- Premenstrual syndrome.
 - Hirsutism due to decreased SHBG.
- Decreased libido.
- Osteoporosis (hypoestrogenism).

Diagnosis of a case of hyperprolactinemia:

1- History:

Of a cause (Drug intake, thyroid, renal...)

Of a symptom (galactorrhea, menstrual problem, ...).

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2- Examination:

- Visual field defect → pituitary adenoma.
- Thyroid → goiter.
- Breast → examined for galactorrhea.
- Chest wall → burn, scar.

3- Investigations:

a- **Prolactin level:** better during the follicular phase, not preceded by intercourse or heavy meal.

- > 100 ng / ml → suggestive of adenoma.
- > 300 ng/ ml → diagnostic of adenoma.
- > 2000 ng/ ml → cavernous sinus invasion.

b- **MRI brain:** - Detect all macroadenoma (> 1cm).
 - Detect 70% of microadenoma(<1cm).

c- **Thyroid function tests.**

d- **Others:**

- Liver function test.
- Kidney function test.

Treatment:

1- Treatment of the cause:

- Treatment of hypothyroidism (thyroxine).
- Stop drugs causing hyperprolactinemia.
- PCO, Liver, renal,

2- Dopamine agonists:

Acts on D2 receptors but also D1, Alpha adrenergic.

Indications: galactorrhea, cases needing fertility, prolactinomas.

Drugs:

1. **Bromocriptine (parlodel):** tablet = 2.5 mg oral or even vaginal.

- Dose: 2.5-10 mg/day start with ½ tablet → ↑ gradually, better during meals.
- Side effects: (D1, adrenergic).
 - 1- Nausea and vomiting.
 - 2- Postural hypotension.
 - 3- Headache.
 - 4- Abdominal cramps.

2. **Lisuride (dopergine):** tablet 0.2 mg

- More potent.
- Less side effects.

3. **Cabergoline (dostinex):** selective D2 agonist tablet 0.5 mg

- Long acting.
- More potent.
- Less side effects.

4. **Quinagolid (norprolac):** non-ergot preparation (D₂ receptors), less side effects.

5. **Vitex agnus castus (Agnucaston):** a herb with prolactin lowering effect.

3- Trans-sphenoid surgery:

For Pituitary adenoma only if:

- No response to medical treatment.
- Causing visual field defect.
- Treatment is not tolerable.

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Abnormal uterine bleeding

It is a symptom not a disease.

Definitions:

Menorrhagia:

- Excessive & / or prolonged menstruation.
- Excessive & / or prolonged cyclic uterine bleeding at regular interval.
- Excessive > 80 ml (↑ amount).
- Prolonged > 7 days (↑ duration) → **Menostaxis**.

Polymenorrhea:

- Too frequent menstruation.
- Menstrual cycle is < 21 days.
- Cyclic bleeding which is normal in amount but with short inter-menstrual interval.

Polymenorrhagia: polymenorrhea + menorrhagia.

- Cyclic bleeding which is excessive & too frequent.

Metrorrhagia: irregular or continuous uterine bleeding not related to menstruation.

Menometrorrhagia: Irregular or acyclic bleeding and of excessive amount.

Breakthrough bleeding: Spotting or mild bleeding during the Intermenstrual (IM) period or during hormonal therapy.

Causes of abnormal uterine bleeding according to age

1) Neonates: slight bleeding during 1st week of life due to withdrawal of estrogen obtained from maternal circulation → “birth crisis”.

2) Childhood:

1. Precocious puberty.
2. F.B. in vagina.
3. Vulvo-vaginitis of childhood.
4. Granulosa cell tumor of ovary.
5. Grape like sarcoma of cervix (sarcoma botryoids).

3) After puberty:

- Dysfunctional uterine bleeding.
- Von Willbrand disease → must be excluded.
- Complication of pregnancy → must be excluded.

4) Child bearing period:

1. **Complication of pregnancy** (commonest in this group): abortion, ectopic pregnancy, vesicular mole, post-abortive

2. **General:**

- Blood disease: leukemia, thrombocytopenia, Von-Willbrand disease, coagulation defect.
- Anti coagulant therapy.
- Thyroid disease:
 - Hypothyroidism.
 - Hyperthyroidism (early).
- Liver disease:
 - ↓ metabolism of estrogen → ↑ E → endometrial hyperplasia → menorrhagia.
 - ↓ SHBG → ↑ free estrogen.
 - ↓ coagulation factors.
- Hypertension.
- Congestive heart failure.
- Obesity.

3. **Local:**

- Traumatic: FB, IUD.
- Inflammation: Erosion, endometritis, salpingitis.

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- Neoplastic: benign, malignant.
- Pelvic congestion: Adenomyosis, displacement (RVF, prolapse), chronic pelvic inflammation, simple congestion (coitus interruptus).

4. Dysfunctional uterine bleeding.

5. Contraception:

- IUCD.
- Irregular use of hormones.
- Tubal sterilization.

5) Premenopausal bleeding "≥ 40y old"

- Dysfunctional uterine bleeding "common".
- Exclude organic causes (fibroid – Cervical tumors – endometrial hyperplasia or carcinoma).

6) Post menopausal bleeding: **see later**

Menorrhagia

Definition:

- Excessive & / or prolonged menstruation.
- Excessive & / or prolonged cyclic uterine bleeding at regular interval.
- Excessive > 80 ml (↑ amount). - Prolonged > 7 days (**Menostaxis**)

Etiology:

1- General causes:

1. Blood disease: leukemia, thrombocytopenia, Von-Willbrand disease, coagulation defect.
2. Anti coagulant therapy.
3. Thyroid disease:
 - Hypothyroidism.
 - Hyperthyroidism (early).
4. Liver disease:
 - ↓ metabolism of estrogen → ↑ E → endometrial hyperplasia → menorrhagia.
 - ↓ SHBG → ↑ free estrogen.
 - ↓ coagulation factors.
5. Hypertension.
6. Congestive heart failure.
7. Obesity.

2- Local causes:

All causes of pelvic congestion:

1. Chronic pelvic infection: PID, chronic cervicitis.
2. Pelvic tumors: fibroid.
3. Displacement: RVF, prolapse.
4. Endometriosis & adenomyosis.
5. Simple pelvic congestion (constipation, coitus interruptus).
6. Extra genital causes → appendicitis.
7. Pelvic congestion syndrome (v.v in broad ligament).

Other causes:

1. IUCD.
2. Tubal sterilization.
3. ↑ surface area of endometrium → bicornuate uterus.

3- Dysfunctional menorrhagia: "Bleeding in the absence of organic cause".

- Irregular ripening of endometrium.
- Irregular shedding of endometrium.

Diagnosis of menorrhagia:

See Investigation of a case of abnormal uterine bleeding.

Treatment: **See later**

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Polymerorrhea

Definition:

- Too frequent menstruation.
- Menstrual cycle is < 21 days.
- Cyclic bleeding which is normal in amount but with short inter-menstrual interval.

Etiology:

- Dysfunctional:** due to hypothalamo-pituitary ovarian axis dysfunction
 - **Short follicular (proliferative) phase:** Early maturation of Graffian follicle due to ovarian hyperstimulation.
 - **Short luteal (secretory) phase:** Early degeneration of corpus luteum due to ovarian congestion as a part of pelvic congestion.
- Other endocrine abnormalities:** e.g. hypothyroidism.

Treatment:

- Treatment of the cause** → Thyroxine for hypothyroidism.
- Progesterone** in 2nd half of cycle:
Norethisterone (primolut N) 10 mg for 10 days starting on day 15th of cycle.
- Combined oral contraceptives** for 21 days each month.

** Hormonal treatment is given for 3 months to prevent recurrence aiming for spontaneous cure.*

Polymerorrhagia: polymerorrhea + menorrhagia.

- Cyclic bleeding which is excessive & too frequent.
- Caused mainly by pelvic congestion (infection).

Metrorrhagia

Definition: irregular or continuous uterine bleeding not related to menstruation.

Etiology:

- Local lesion in genital tract:** "the commonest"
 - Cervical erosion.
 - Cervical polyp, ulcer.
 - Cervical cancer.
 - Fibroid polyp with necrosed tip.
 - Endometrial carcinoma.
 - Sarcoma.
 - Feminizing ovarian tumor.
 - Trauma: retained pessary, F.B.
- Irregular use of hormones/ pills.**
- IUCD.**
- Dysfunctional ut. bleeding (acyclic anovular).**
- Complication of pregnancy:** abortion, ectopic pr., vesicular mole

*** Menometrorrhagia:** Irregular or acyclic bleeding and of excessive amount.

Dysfunctional uterine bleeding

Definition: It is abnormal uterine bleeding in absence of any systemic or organic cause in the genital tract.

Age:

- Before menopause (50%):**
 - ↓ number of follicles.
 - ↑ resistance to gonadotrophins.
 - After puberty (20%):** immaturity of hypothalamo-pituitary- ovarian axis.
 - At any time between puberty & menopause.**
-

II. Reproductive endocrinology and infertility

Classification:

1- Histological

- **Ovular:** "secretory changes in endometrium"
- **Anovular:** "No secretory changes"

2- Clinical

▪ **Cyclic**

- Polymenorrhea.
- Menorrhagia.

▪ **Acyclic**

- Threshold bleeding.
- Simple anovulation.
- PCO.

I-Ovular (acyclic)

1- Dysfunctional polymenorrhea

- Short cycle due to:
 - * short proliferative phase.
 - * short secretory phase.
- Tendency to spontaneous cure.
- Treatment: *see before* (progesterone- COP).

2- Dysfunctional menorrhagia

(A) Irregular ripening of endometrium:

- Poor formation & function of corpus luteum → the endometrium is without adequate hormonal support → bleeding starts several days **before** menstruation.
- Premenstrual endometrial biopsy → weak secretory changes.
- Treatment: progesterone: 10 mg norethisteron for 10 days starting from 15th day of cycle.

(B) Irregular shedding of endometrium:

- Slow & incomplete degeneration of corpus luteum → bleeding continues for several days after proper flow.
- Endometrial biopsy on 5th day of menstruation → shows areas of secretory endometrium while it should be early proliferative.
- Treatment is "difficult"
- Oral contraceptive pills for 3 cycles to inhibit ovulation & corpus luteum formation.

II-Anovular (acyclic):

-A semiquantitative relationship exists between the amount of estrogen available to stimulate the endometrium and the type of bleeding that can occur.

(A) PCO: This is one of the common causes of irregular vaginal bleeding with short periods of amenorrhea followed by periods of bleeding (*see before*).

(B) Estrogen breakthrough bleeding:

1- Threshold bleeding

- Relatively low levels of estrogen yield intermittent spotting that may be prolonged but is generally light in amount.
- The ovary produces small amount of oestrogen that fluctuates above & below the threshold level required to support endometrium.
- Endometrial biopsy:
 - Thin endometrium.

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→ Poorly developed proliferative phase.

- Treatment:

→ Estrogen for 21 days.

→ Progesterone added in last week

***N.B.:** suggested level of estrogen associated with bleeding is 50-100 pg/ml.

2- Simple anovulation: Metropathia hemorrhagica (Schroeder's disease)

Definition: It is acyclic anovular bleeding from hyperplastic endometrium characterized by prolonged, painless, excessive bleeding after a short period of amenorrhea.

Etiology: Unknown

- Graffian follicle fails to rupture & continue to grow to form a cyst or not.

- It secretes large amount of estrogen which acts on uterus:

→ Short period of amenorrhea.

→ Endometrial hyperplasia.

→ Myometrial hypertrophy.

- Then:

→ When estrogen reaches ↑ level → ↓ FSH secretion → degeneration of Graffian follicle.

→ Exhaustion of graffian follicle.

- So → estrogen withdrawal bleeding.

Pathology:

1- Uterus:

*** Gross:**

- Symetrically enlarged, soft (↑ vascularity).

- Myometrial hypertrophy.

- Endometrium → thickened, polypoidal, hyperplastic.

*** MIC:**

Proliferative or "Endometrial hyperplasia"

- ↑ size & number of glands which become cystic "Swiss cheese appearance".

- Stroma → dense & oedematous.

- No secretory changes.

2- Ovaries:

- Enlarged & cystic → large graffian follicle or multiple small follicular cysts (< 5cm).

- Lined by granulosa cells.

- No corpus luteum.

Diagnosis:

- Short period of amenorrhea followed by bleeding: Prolonged, Excessive, Painless.

- U/S → Thickened endometrium, myometrium.

- Hysteroscopy → visualize endometrium & obtain biopsy.

- Endometrial biopsy → Simple endometrial hyperplasia (cystic glandular hyperplasia).

Treatment: Suppression by pills, then induction of ovulation if there is desire for fertility or continue suppression if no desire.

II. Reproductive endocrinology and infertility

Investigations of a case of abnormal uterine bleeding

(I) History:

1. Personal history:
 - * Age:
 - After puberty → dysfunctional uterine bleeding.
 - Before menopause → dysfunctional uterine bleeding.
 - Reproductive age → pregnancy complication.
 - > 40y → suspect malignancy.
 - * Marital status: pregnancy complication.
2. Present history:
 - * Amount, character, duration of bleeding.
 - * Cyclic or acyclic bleeding.
 - * Associated symptoms (pain- discharge).
3. Past history:
 - * General disease: HPN, CHF, bleeding tendency.
 - * Drugs: pills.
4. Menstrual history: before bleeding. Short period of amenorrhea (PCO- simple anovulation - pregnancy complication).
5. Obstetric history:
 - Recent abortion or labor → dysfunctional uterine bleeding.
 - Recent vesicular mole → Choriocarcinoma.

(II) General examination:

- Degree of anemia.
- Presence of cachexia: malignant tumor.
- Signs of bleeding disorder.
- General disease: HPN, thyroid.

(III) Abdominal examination:

Pelvi- abdominal mass (pregnancy- fibroid- ovarian tumors).

(IV) Pelvic examination:

- Exclude urethral & anal cause of bleeding.
- Detect local cause: vaginal, cervical, fibroid.
- Inspection of vulva for masses, ulcers.
- P/V → vaginal & cervical masses.
- Bimanual examination for (uterine- ovarian) masses.
- Speculum examination → cervical lesion.
- P/R → rectum, parametrium.

(V) Special investigations:

Imaging:

1. Transvaginal ultrasonography (TVS):
 - Ovarian masses.
 - Uterine fibroid, endometrial carcinoma.
2. HSG: uterine polyp.
3. MRI: imaging uterus & endometrium.
 - * detect small masses.
 - * degree of invasion of myometrium in cases of endometrial carcinoma.

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Laboratory tests:

- CBC.
- Bleeding time, coagulation time.
- Thyroid function test.
- Liver function.
- Serum progesterone on day 22 → LPD.
- β hCG.

Endoscopy:

1. Hysteroscopy:
 - Uterine polyp.
 - Endometrial mass.
2. Laparoscopy: may reveal oestrogen secreting tumor if small.

Malignancy work up:

1. Endometrial biopsy: in every woman > 40 to diagnose:

- Endometrial carcinoma.
- Endocervical carcinoma.
- DUB.

*** Methods:**

- Fractional curettage.
- Hysteroscopic.
- Endometrial aspiration.

2. Test to detect cancer cervix:

- Cervical smear.
- Colposcopy.
- Biopsy.

Treatment of abnormal uterine bleeding

1) General treatment:

- Correct anemia "iron & vitamin".
- Blood transfusion in severe cases.
- Correct bleeding disorders.
- Liver support in liver diseases.
- Correct thyroid disorders.

(2) Treatment of the cause: myomectomy, polypectomy.....etc.

(3) Medical "non hormonal" treatment:

1. Anti-fibrinolytic:

- EACA "epsilon- amino- caproic acid": 3 gm 4-6 time.
- Tramexamic acid → 1gm tds.
- ↓ Blood loss by 50%.

2. Anti-prostaglandins:

- Mefenamic acid (ponstan): 250- 500 mg tds.
- Ibuprofen (Brufen): 400mg tds.
- ↓ PGE
- Blood loss is reduced by 25-50 %.

3. Hemostatics:

- Diosmin (Daflon) 500 mg 2 × 2
- Ethamsylate (Dicynon) 500 mg 2 × 2.
- ↓ Capillary fragility.
- ↑ platelet aggregation.

(4) Hormonal treatment: → mainly for DUB.

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1. Progesterone:

Cyclic fashion:

- Starting at 15th day of cycle for 10 days in ovulatory cases.
- Starting at 5th day of cycle for 20 days in anovulatory cases. When treatment is stopped → shedding of endometrium (medical curettage).
 - Norethisterone (Primolut N) tablets Dose is 10- 15 mg
 - Medroxyprogesterone acetate (provera tablet) Dose is 10 mg daily

2. Combined estrogen & progesterone:

- 2-3 tablets are given everyday till bleeding stops then 1 tablet/ day → 20 days.
- Given in usual way for 3 months.

3. Estrogen: in cases of acute sever hemorrhage.

- If bleeding is heavy: conjugated estrogen → 12.5mg IV/ 12 hours "2 doses"
→ induce growth of endometrium → stop bleeding.
- It should be followed by:
 - Combined E & P.
 - Progesterone.

4. Androgens: it controls bleeding but → virilization:

Danazol: weak synthetic androgen

- 200- 400 mg → 3 month.
- expensive, androgenic.

- Used when (E & P are contraindicated- intractable menorrhagia).

Gesterinone: 2.5mg twice weekly → 3 months

- Androgenic.
- Anti-P.
- Anti-E.

5. GnRH analogues:

- Lead to amenorrhea.
- Intranasal, S.C, IM / month for 3 successive months.
- Intractable menorrhagia.

6. Progesterone- levonorgestrel IUD: (Mirena)

- Reduce blood loss by 80%.
- Used in cases of liver failure, chronic renal failure.

7. Induction of ovulation:

- In case of anovulation & pregnancy is desired.

(5) Surgical treatment:

1. Dilatation & curettage:

* Indication:

- 1) Severe bleeding.
- 2) Failure of medical treatment.
- 3) Patient > 40 years to exclude organic disease.

* Value:

- 1) Diagnose organic lesions: endometrial hyperplasia & endometrial carcinoma.
- 2) Determine type of dysfunction.
- 3) Therapeutic: ↓ bleeding by 60%.

2. Hysterectomy:

- * Failure of all measures.
- * Patient > 40y & completed her family.

3. Endometrial ablation: "alternative to hysterectomy"

* Indication:

II. Reproductive endocrinology and infertility

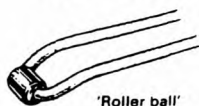
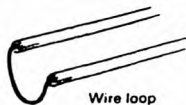
- 1) Patient unfit for hysterectomy.
- 2) Young PT wants to preserve uterus.

*** Contraindication:**

- 1) Intra uterine pathology.
- 2) Uterus > 12 wk.
- 3) Infection.

*** Methods: (Hysteroscopic guided)**

- Diathermy resectoscopic.
- Laser.
- Thermal.



Post-menopausal bleeding

Definition: bleeding from genital tract 6 month - 1 year after menopause.

Menstruation continuing after age of 55y should be investigated.

Causes: the commonest cause is → withdrawal bleeding of estrogen used in HRT.

1- Estrogen therapy (25%).

2- General cause:

1. Blood disease.
2. Anticoagulant therapy.
3. Ginseng (in some tonics) has some estrogenic effect → may cause bleeding.

3- Local causes:

1. Malignant lesions:

- Endometrial carcinoma.
- Sarcoma.
- Ovarian tumours.

2. Non-malignant lesions:

- Urethral caruncle.
- Senile vaginitis.
- Senile endometritis.
- FB (retained pessary).

4- Idiopathic (Atrophic endometritis): (15%)

Diagnosis:

"All cases are considered malignant till proved otherwise"

"Malignancy is not the commonest cause but the most serious cause and therefore should be excluded first"

(1) History:

1. Personal history: endometrial cancer common in 55- 70 y.
2. Present history:
 - amount, character, duration of bleeding.
 - associated symptoms (pain, discharge).
3. Past history:
 - DM, HPN, cardiac.
 - Estrogen therapy.
4. Family history: endometrial cancer, ovarian cancer.
5. Obstetric history: parity:
 - Nullipara → endometrial cancer, ovarian cancer.
 - Multipara → cervical cancer.

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(2) Examination:

1. General examination: anemia, bleeding tendency, general disease, cachexia, metastasis.
2. Abdominal examination: pelvi-abdominal mass:
 - Ovarian tumor.
 - Pyometra- hematometra.
 - Cervical & uterine tumors.
3. Pelvic examination:
 - Exclude urethral & anal cause of bleeding.
 - Inspection of vulva for masses, ulcers.
 - P/V: vaginal & cervical masses.
 - Bimanual examination for (uterine- ovarian) masses.
 - Speculum examination → cervical lesion.
 - P/R → rectum, parametrium.

(3) Special investigations:

1. Transvaginal U/S (TVS):
 - Endometrial thickness.
 - Endometrial cancer.
 - Ovarian masses.
2. Cervical & vaginal smear.
3. Endometrial biopsy: It must be done in all cases to exclude endometrial carcinoma:
 - A- Fractional curettage: specimen from the cervix & body of the uterus → endocervical, endometrial Ca.
 - B- Endometrial aspiration: Vabra aspirator, pipelle curette.
 - Without anaesthesia.
 - ↓ Complication (perforation).
 - ↓ Cost.
 - Detect 96% of endometrial Ca.
 - C- Hysteroscopy: visualize the cervical & uterine cavities followed by curettage or directed biopsy.
4. Biopsy: from any suspected lesion.
5. Laboratory:
 - Thyroid function testes.
 - Liver function testes.
 - CBC.
 - Bleeding & coagulation time.
6. Hysteroscopy:
 - Uterine polyp.
 - Endometrial mass.
7. MRI: imaging uterus & endometrium.
 - detect small masses.
 - degree of invasion of myometrium in cases of endometrial carcinoma.
8. Laparoscopy:
 - It may reveal oestrogen secreting tumor if small.
 - It may be used for surgical staging.

* Treatment: Treatment of the cause.

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Dysmenorrhoea

Definition: Dysmenorrhea means pain related to menstruation.

Types:

Spasmodic dysmenorrhea.

Membranous dysmenorrhea.

Congestive dysmenorrhea.

Primary (spasmodic, idiopathic) dysmenorrhoea

It is a common complaint in young girls (teenagers). Pain occurs in absence of any organic pelvic lesion.

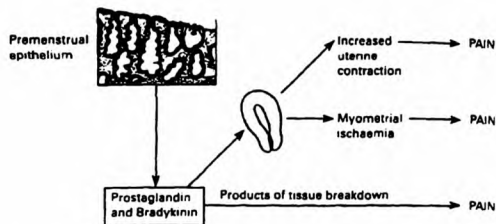
Etiology: Spasmodic dysmenorrhea is explained by more than one theory because not all cases arise in the same way.

- 1) Prostaglandin effect is **the most accepted theory**. In primary dysmenorrhea there is increased production of prostaglandin $F_{2\alpha}$ in the endometrium. It causes vasoconstriction and uterine ischemia which may cause the pain of dysmenorrhea. It also causes strong uterine contractions (uterine spasm). Progesterone stimulates the production of prostaglandins in the endometrium and so anovulatory cycles are painless. The production of prostaglandin reaches a peak at, or soon after, the start of menstruation, with the onset of bleeding, the formed prostaglandins are released from the shedding endometrium.
- 2) **Hormonal imbalance.** Relative excess of progesterone causes contraction of the uterine isthmus and formation of a thick endometrium which is difficult to be expelled through the cervix. Anovulatory cycles are painless due to absence of progesterone.
- 3) **Cervical obstruction;** due to cervical stenosis or retroflexion of the uterus. This causes retention of menstrual blood. The retained blood causes irregular and painful contractions. Also there may be increased reabsorption of prostaglandins from retained blood. At the same time blood may regurgitate along the tubes into the peritoneal cavity leading to peritoneal irritation and pelvic pain.
- 4) **Uterine hypoplasia.** The underdeveloped muscle is unable to expel the blood which accumulates causing dysmenorrhea.
- 5) **Low pain threshold.**
- 6) **Ischemia of uterine muscle,** resulting in pain similar to that of angina pectoris.
- 7) **Hypersensitivity of the sympathetic nerve fibres of the uterus.**
- 8) **Disturbed polarity of the uterus.** Uterine polarity means when the fundus contracts the cervix dilates and vice versa dilatation of cervix reflexly causes uterine contraction. The disturbed polarity leads to difficulty in discharge of menstrual blood resulting in pain.
- 9) **Clotting of menstrual blood.** The clots are difficult to expel. However clots may be passed without causing pain.
- 10) **General causes:**
 - Psychological disturbances.
 - S. This may release prostaglandins within the uterus.

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Clinical picture:

- **Age:** It usually starts 1 or 2 years after menarche because the first cycles are usually anovulatory. This dysmenorrhea occurs only in ovulatory cycles and usually improves after the age of 25.
- **Parity:** Pain improves or disappears after an abortion or labour because dilatation of the cervix causes laceration of the nerve fibres which transmit pain.
- **Family History:** There is increased incidence among mothers and sisters of women with primary dysmenorrhea.
- **Type of Pain:** Pain starts on the first day of menstruation, reaches its maximum within 24 hours while the bleeding is slight, and then improves when the flow becomes established. In few cases pain is felt through the whole period. Pain is colicky, intermittent, felt in the suprapubic region and is often referred to the inner and front sides of the thighs.
- **Associated Symptoms:** Nausea, vomiting, diarrhea, and urinary disturbances may accompany pain.



Treatment:

1. General Treatment:

- a. Explanation and reassurance of the patient.
- b. Avoid sedentary life and encourage muscular exercises.
- c. Treatment of constipation and restriction of coffee.
- d. Yoga and acupuncture may be tried.

2. Non-hormonal Treatment:

- 1) Antiprostaglandins which inhibit the synthesis of prostaglandins as naproxen or ibuprofen (Brufen tablets 400 mg thrice daily during the period). Pain is relieved in 80% of cases.
- 2) Antispasmodics.

3. Hormonal Treatment:

Indicated when medical treatment fails. The main idea is to inhibit ovulation because anovulatory cycles are painless. Hormonal treatment is given for 6-12 successive months. Combined contraceptive tablets to inhibit ovulation. Pain is relieved in 90% of cases.

4. Surgical Treatment: Indicated when hormonal treatment fails.

- **Dilatation of the cervix.** The cervix is dilated to 10 mm (No 10 Hegar dilator). Dilatation causing laceration of the nerve fibres around the internal os which transmit pain.
- **Presacral sympathectomy (neurectomy).** Indicated when all other measures fail. It is an abdominal operation to remove the presacral nerve or plexus of nerves lying in front of the 4th, 5th lumbar vertebrae and sacral promontory. Operation is done by laparotomy or laparoscopy.
- **Laser uterine nerve ablation (LUNA).** Through laparoscopy, laser is used to divide the uterosacral ligaments containing the nerve supply of the uterus. It is done alternative to presacral neurectomy.

II. Reproductive endocrinology and infertility

Membranous dysmenorrhoea

It is a rare type of spasmodic dysmenorrhea in which pain is very severe and is relieved after the passage of an endometrial cast during the third or fourth day of menstruation.

Typically, the cast is triangular in shape but sometimes, it is passed in the form of 2 or more large fragments.

Treatment is like spasmodic dysmenorrhea in addition to repeated curettage to remove the unhealthy endometrium.

Secondary (congestive) dysmenorrhoea

Etiology: Pain is due to pelvic congestion which is caused by:

- Chronic pelvic infection as cervicitis, endometritis or salpingitis.
- Pelvic tumours as fibroids or ovarian cyst.
- Abnormal position of the uterus as retroversion or prolapse.
- Simple pelvic congestion due to chronic constipation or coitus interruptus.
- Pelvic congestion syndrome due to broad ligament varicocele.
- Endometriosis and adenomyosis lead to a specific type of dysmenorrhea.
- Extragenital lesions as chronic appendicitis.

Clinical Picture:

- Age: It usually occurs after the age of 30.
- Parity: More in parous women.
- Type of Pain: Pain starts several days (3-5 days) before the period, increases gradually as menstruation approaches and is relieved by the onset of the flow due to diminution of pelvic congestion. In some cases the pain is felt through the whole period. The pain is a continuous dull ache felt in the lower abdomen and accompanied with backache.
- Associated Symptoms: Menorrhagia, Polymenorrhea and increased normal vaginal discharge (leucorrhoea).

Treatment:

- Treatment of the cause.
- Analgesics.
- Measures to relieve pelvic congestion as ichthyl in glycerin vaginal pessaries, warm vaginal douches. Ichthyl is soothing of pain, and glycerin is hygroscopic and relieves congestion.

Mittelschmerz or ovulation pain:

Clinical picture:

- It is a midcycle dull aching pain felt in one or other iliac fossa about the time of ovulation.
- It lasts for a few hours rarely longer than 24 hours.
- Sometimes accompanied with nausea and vomiting.
- Pain may be severe and mistaken for appendicitis or acute abdominal conditions.
- Occasionally it is accompanied by increased vaginal discharge or slight vaginal bleeding (ovulation bleeding) which is due to a fall in the level of estrogen at the time of ovulation.

Etiology: The pain may be due to:

- **Increased tension** within the ovary due to a thickened tunica albuginea which interferes with rupture of the Graafian follicle at the time of ovulation (preovulatory).

II. Reproductive endocrinology and infertility

- **Peritonism:** Irritation of the peritoneum by fluid or blood from the ruptured follicle (ovulatory).
- **Tubal contractions:** The tube shows active contractions at the time of ovulation (Prostaglandin effect) which may cause pain (postovulatory).

Treatment:

- Explanation and reassurance.
- Analgesics.
- Temporary inhibition of ovulation by contraceptive tablets given for 3 months. Spontaneous cure is always liable to occur.

Premenstrual syndrome

Definitions:

- **Premenstrual syndrome (PMS)** means cyclic recurrence of psychological, behavioral, or somatic symptoms during the luteal phase of the menstrual cycle and in absence of organic disease. Symptoms occur only in ovulatory cycles and are relieved by the end of menstruation.
- **Premenstrual dysphoric disorder (PMDD):** characterized by depressed or labile mood, anxiety, irritability, anger, and other symptoms occurring exclusively during the 2 weeks preceding menses. The symptoms must be severe enough to interfere with occupational and social functioning, in contrast with the more common PMS. PMDD is a severely distressing and disabling condition that requires treatment.

Etiology:

The actual cause is unknown and the syndrome may be attributed to:

- 1) Lack of serotonin (a neurotransmitter) mediated by the fluctuations of the levels of sex hormones (progesterone, estrogen, and testosterone) in the luteal phase of the menstrual cycle.
- 2) Variants in the estrogen receptor alpha gene are associated with PMDD. Women with these genetic variants are more likely to suffer from PMDD.
- 3) High oestrogen levels, or low progesterone levels, i.e., high oestrogen-progesterone ratio. Progesterone stimulates sodium loss thus preventing water retention, and has a sedative effect on the central nervous system.
- 4) Allergic reaction to the corpus luteum so the syndrome is seen only with ovulatory cycles.
- 5) Increased secretion of aldosterone which leads to salt and water retention.
- 6) Increased antidiuretic hormone leading to water retention.
- 7) Elevated serum prolactin.
- 8) Endorphin Theory: There is a decrease in the level of beta-endorphins in the luteal phase. These endogenous opiates are associated with a sense of well-being.
- 9) Psychological Disturbances

Symptoms:

- 1- Nervous symptoms: headache, migraine, palpitation, irritability, depression and insomnia.
- 2- Behavioral symptoms: as poor concentration, bad performance.
- 3- Gastrointestinal symptoms: as nausea, vomiting, diarrhea, or constipation.
- 4- Mastalgia which means swelling and pain of the breasts.
- 5- Water retention manifested by edema of the face, eyelids, and legs.

II. Reproductive endocrinology and infertility

Treatment:

The primary goal of treatment is to reduce the patient's suffering and the disruption to her social relationships.

- Explanation and reassurance.
- Symptomatic treatment: tranquilizers for irritability.
- Moderate exercise may be helpful by increasing production of endogenous endorphins.
- Selective serotonin reuptake inhibitors (SSRIs) have emerged as first-line therapy. The U.S. Food and Drug Administration (FDA) has approved four SSRIs for the treatment of PMDD: Fluoxetine (available as generic or as Prozac or Sarafem), sertraline (Zoloft), paroxetine (Paxil) and escitalopram oxalate (Lexapro).
- Restriction of salt for 7-10 days premenstrual to reduce fluid retention.
- Diuretics: Spironolactone (Aldactone) is the diuretic of choice.
- Progestogens. To improve luteal phase deficiency.
- Bromocriptine (Parlodel) or Lisuride (Dopergin) tablets to inhibit prolactin secretion. It is tried if the main complaint is mastalgia.
- Vitamin B6 (pyridoxine): It increases the synthesis of dopamine which is the prolactin-inhibiting hormone.
- Inhibition of ovulation: This is **the most appropriate treatment** and is achieved by: Combined oral contraceptives.
- Psychotherapy for resistant cases.

II. Reproductive endocrinology and infertility

Infertility

Definition:

It is inability to conceive after a reasonable period (1-2 years) of continuous married life without use of contraception.

Sterility is failure of conception due to non-treatable cause (e.g. absence of uterus).

The most important determinant of a couple's fertility is the woman's age.

Incidence: 10-15% of couples are infertile.

Types:

- **1st infertility:** Conception has never occurred.
- **2nd infertility:** Conception has occurred once or more before.

Etiology:

- Female factor: (40-55%):
 - **Ovarian** cause: (30-40%).
 - **Tubal** cause: (30%).
 - **Peritoneal** cause: (5-10%).
 - **Uterine** cause: (5-10%).
 - **Others:** vaginal, cervical.
- Male factor: 30-40%.
- Unexplained infertility: 15%.
- Disturbance of sexual relation.
- Both male and female: 10%.

Female factor of infertility

(1) Ovarian factor of infertility (30%)

It includes: anovulation, luteal phase defect and luteinized unruptured follicle

(A) Anovulation:

Anovulation refers to menstrual arrhythmia that results from disruption of the CNS-hypothalamic-pituitary-ovarian-endometrial axis. It is manifested clinically as amenorrhea, menstrual acyclicity or

h i r s u t i s m

Causes: It is the commonest cause of 1st infertility in females.

1. **WHO group I:** Central (low or low normal FSH).
2. **WHO group II:** Ovarian dysfunction mainly PCO.
3. **WHO group III:** Gonadal failure. (high FSH)
4. **WHO group IV:** Hyperprolactinemic anovulation.

Detection of ovulation:

▪ Symptoms suggestive of ovulation:

- Regular cycles.
- Spasmodic dysmenorrhea.
- Premenstrual syndrome.
- Ovulatory pain.
- Ovulatory discharge.
- Ovulatory spotting.

▪ Tests to detect ovulation:

1. Basal body temperature:

- It depends on the presence of functioning corpus luteum → progesterone which is indicator of ovulation.

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- Progesterone has thermogenic effect → ↑ temperature 0.2-0.4°C in 2nd half of cycle (biphasic curve).
- Patient: record temperature in the morning (rectal or oral, record any infection).
- In anovulatory cycle, curve is monophasic.

II. Hormonal assay:

- Midluteal serum progesterone (depending on cycle length: usually day 21-23).
- < 3 ng/ml → anovulation 3-10 ng/ml → luteal phase defect
- > 10 ng/ml → ovulation + normal corpus luteum function
- Detection of LH in urine occurs 36 hours before ovulation.

III. Ultrasound:

Serial transvaginal ultrasound (folliculo-metry) → preovulatory Graffian follicle 18-22 mm.

IV. Premenstrual endometrial biopsy:

- Taken 1-2 days before expected day of the cycle.
- One or 2 strips of endometrium is taken from fundus by Pirelli without anesthesia or dilatation with no harm to ongoing pregnancy.
- Value:
 - **Diagnosis of ovulation:** Secretory endometrium.
 - **Luteal phase defect:** Lag of 2 or more days compared to biopsy.

V. Cervical mucus:

- -ve fern test after being positive.
- -ve Spinnbarkeit test (thread test) after being positive.

- *Once anovulation was diagnosed, we try to find the cause:*

Group I: FSH level < 5 mIU/ml: Hypothalamic/pituitary cause.

Group II: 17α-hydroxyprogesterone → congenital adrenal hyperplasia.

FSH and LH.

Androgens (testosterone, androstenedione, DHEA and DHEAS).

Group III: FSH > 40 mIU/ml: Ovarian failure.

Group IV: Prolactin level and thyroid function.

Ovarian reserve test: AntiMüllerian Hormone (AMH) in cases with advanced age or history of prior ovarian surgery.

Treatment:

General treatment: Proper diet (malnutrition or obesity).

Treatment of the cause: Bromocriptine → Hyperprolactinemia.

Induction of ovulation (medical and surgical).

Induction of ovulation

(1) Clomiphene citrate (Clomid):

Clomid needs intact hypothalamus-pituitary-ovarian axis. So, it is indicated in cases with type II anovulation.

It is synthetic non-steroidal compound → anti-estrogenic. Cyclofenil or tamoxifen is anti-estrogen similar mechanism to clomiphene.

Mechanism:

- It competes with the endogenous estrogen for the estrogen receptors in the hypothalamus resulting in false sensation of decreased estrogen level.
 - The hypothalamus is then released from the negative feedback of estrogen.
 - GnRH is produced from the hypothalamus releasing pituitary gonadotropins (FSH).

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- FSH stimulates the follicles leading to production of estradiol.
- When the clomiphene citrate is stopped, the estradiol produced from the follicles induce positive feedback on the hypothalamus with subsequent LH surge and hence ovulation occurs.
- It competes with the endogenous estrogen for the estrogen receptors in the genital tract especially the cervix (producing poor quality cervical mucus).

Other indications:

1- LPD.

2- Treatment of oligospermia in males.

▪ Contraindications:

Liver disorder.

▪ Visual disturbances on previous use of clomiphene citrate.

Dose:

1- 50-250 mg/day for 5 days.

2- Starting from:

- 2nd – 5th day of menstrual cycle **or**

- 5th day of progesterone withdrawal bleeding in case of amenorrhea.

3- We monitor therapy by:

- Folliculometry.

- Day 21 progesterone.

4- We may add small dose of estrogen for 5 days from 10th day to counteract action on cervical mucus.

5- Maximum is 6 cycles.

Success rate:

Ovulation (75%) occurs 5-9 days after stopping Clomid. While pregnancy occurs in 40-50%.

Side effects:

2- Multiple pregnancy (5-10%) → Increased risk of abortion.

3- Ovarian hyperstimulation syndrome (1-2%) → Liable to occur with PCO, so start with 50 mg/day.

4- Headache.

5- Nausea and vomiting.

6- Breast tenderness.

7- Visual disturbance (mydriatic effect).

8- Decreased quality of cervical mucus and endometrium (LPD).

Clomid resistance is no ovulation for 3-4 cycles with increasing dose from 50- 250 mg.

Clomid failure occurs in women who do not conceive despite clomid-induced ovulation.

Clomid pregnancy failure: Pregnancy occurs followed by abortion.

(2) Human Menopausal Gonadotrophins (HMG):

It is prepared from urine of menopausal females.

Indications:

1- Anovulation (WHO group 1).

2- Anovulation (WHO group 2).

3- Clomid failure.

4- Luteal phase defect.

5- For production of superovulation for IVF and IUI.

6- In males, oligospermia.

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Dose:

- Each ampoule contains 75 IU FSH and 75 IU LH.
- 1-2 ampoules every day from 2nd day of cycle.
- Monitor therapy by:
 - Folliculometry.
 - Estradiol level.
- When follicle ≥ 18 mm and E2 1000-1500 pg/ml, give ovulatory dose of HCG (5000-10,000 IU) IM.

Result:

Ovulation occurs > 90% per cycle.

Side effects:

- Ovarian hyperstimulation (1-6%).
- Multiple pregnancy (25%).

(3) Pure FSH (Fostimon) is used in cases of PCO.

(4) Gonadotrophin Releasing Hormone (GnRH):

Not in current practice.

(5) Aromatase inhibitors:

Letrozole (Femara) 5 mg/day for 5 days decreases peripheral E production leading to increased FSH which stimulates ovarian follicle development.

(6) Combination of clomiphene + hCG or HMG + hCG.

hCG is prepared from urine of pregnant female and it is given after stimulation by clomiphene (when follicle > 22 mm) or HMG (≥ 18 mm).

- hCG dose is 5,000-10,000 IU IM.
- hCG resembles mid-cycle LH surge and triggers ovulation 34-36 hours following injection.

Ovarian hyperstimulation syndrome

It is a serious condition and may be life-threatening particularly if the patient got pregnant especially multiple. It is common with HMG and rare with Clomid. It starts 3-6 days after injection of HCG.

Pathogenesis:

- Increased permeability \rightarrow Shift of fluid from intravascular to extravascular space.
- Ascitis and occasional hydrothorax, hemoconcentration and hypovolemia \rightarrow Decreased renal blood flow leading to oliguria and even anuria.

Clinically:

- Mild: Ovarian enlargement + No cyst + Discomfort + Weight gain.
- Moderate: Ovarian cyst (5-12 cm) + N, V, D and \uparrow weight.
- Severe: Abdominal pain + Ascitis + Pleural effusion (hypotension + electrolyte disturbance which may be life threatening) + Hematocrit > 44%.

Types:

- Early: Starts 3-7 days post-hCG.
- Late: Starts 12-14 days post-hCG (pregnancy).

Prevention:

- Careful monitoring specially PCO.
- Decreased dose of HCG in PCO to 5000 IU.

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- Coasting (delay in hCG administration 1-3 days until plateau or decrease in E2 to < 3000 pg/ml).
- Cancellation of the cycle if E2 > 3000 pg/ml.
- Oral cabergoline (decreased permeability).
- Progesterone instead of hCG for luteal support.

Treatment:

- Supportive:
 - * Anticoagulation.
 - * Albumin.
 - * Fluids.
 - * Symptomatic (analgesic, antiemetic, corticosteroid).
- Observation only in mild cases.
- ICU in severe cases.

(B) Luteal phase defect:

Definition:

Decreased production of progesterone by corpus luteum or short luteal phase.

Etiology:

- Hypothalamic or pituitary defect decreases follicular maturation.
- Hyperprolactinaemia.
- Hypothyroidism.
- Hyperandrogenaemia.
- Decreased progesterone receptor on endometrium.
- Endometriosis (\uparrow PGF₂ \rightarrow Lysis of corpus luteum).
- Drugs:
 - * Prolonged synthetic progesterone use.
 - * Androgen.
 - * Clomid.
- Endometrial defects (endometritis and decreased vascularity).

Diagnosis:

Clinically:

- Dysfunctional menorrhagia (irregular ripening).
- Polymenorrhea.
- Infertility.
- Recurrent abortion.

Basal body temperature:

- Biphasic.
- Short luteal phase < 11 days.

Premenstrual endometrial biopsy:

Lag > 2 days when compared to day of biopsy.

Serum progesterone level (days 21-22): 3-10 ng/ml.

To detect cause, prolactin level and thyroid function.

Treatment: According to the cause:

- *Bromocriptine* in case with hyperprolactinaemia.
- *Corticosteroids* in cases with elevated DHEAS.
- *Natural progesterone supplementation* 200 mg twice daily 2 days after rise of body temperature. If pregnancy occurs, continue till 12 weeks.
- *HCG* 2500 IU twice weekly in 2nd half of cycle to maintain corpus luteum function.
- *Induction(augmentation)of ovulation* \rightarrow \uparrow FSH \rightarrow \uparrow Follicular maturation.

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(C) Luteinized Unruptured Follicle (LUF):

It is failure of mature Graafian follicle to rupture followed by luteinization of its cells → Progesterone.

Serum progesterone, basal body temperature and premenstrual endometrial biopsy → Similar to ovulatory cycles.

It is caused by endometriosis and antiprostaglandin use.

U/S three days after LH surge shows failure of Graafian follicle to collapse.

Treatment: Induction of ovulation.

(2) Tubal factor (30%)

The commonest cause of 2nd infertility in females.

Causes: Bilateral tubal block or dysfunction.

Inflammatory: The commonest cause, mostly due to Chlamydia and gonorrhea which cause tubal block or peritubal adhesions leading to kink of tube.

Iatrogenic: Trauma during pelvic surgery or tubal ligation.

Congenital: Non canalization.

Neoplastic: Bilateral cornual fibroid.

Investigations (tubal patency tests): Currently accepted investigations can only test tubal patency not tubal function.

1- Hysterosalpingography. 2- Laparoscopy. 3- Sonohysterography.

4- Tubal insufflation (Rubin test) → Obsolete.

5- Kymography → Obsolete.

(1) Hysterosalpingography

Idea: Injection of contrast medium through transcervical cannula into uterus and imaging of uterus, tubes and peritoneal spill using X-ray.

Contrast medium (urograffin):

- It is water soluble while oil-based media are obsolete.
- 40% iodine + water.
- Avoids oil embolism.
- Second film is after 10-15 minutes.

Timing: 2-5 days after the end of menstruation.

Technique: No anaesthesia is usually needed, analgesia may be given before the procedure. Special cannula is introduced into cervix and 6-8 ml of dye is injected into uterus. X-ray film is taken immediately with follow up of the dye on a special monitor, then 2nd film after 10-15 minutes (for documentation).

Value:

- Shows uterine anomalies; hypoplasia, bicornuate uterus.
- Submucous fibroid (Filling defect).
- Intrauterine adhesions.
- Localize tubal block.
- Detect peritoneal adhesions



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Contraindications:

- Pregnancy and during amenorrhea.
- During bleeding and menstruation (embolism).
- Premenstrual (avoid: embolism, endometriosis, false -ve result and disturb possible pregnancy).
- Pelvic infection (cervicitis, vaginitis, PID or TB).

Complications:

- Vasovagal effects (nausea, vomiting and collapse).
- Infection (ascending infection and flare up of infection).
- Cervical lacerations.

(2) Laparoscopy

Principle: Tubal patency is assessed by injection of methylene blue through cervix (chromotubation). Then visualization of the dye comes out through fimbrial end.

Indication:

- HSG revealed tubal block or peritubal adhesions.
- If all investigations showed no abnormality, no pregnancy occurred for 6 months.

(3) Sonohysterography

[Hysterosalpingo-Contrast Sonography (HyCoSy)]

Idea:

- Echovist (contrast medium) solution or saline is injected into uterus through cervix.
- TVS or transabdominal U/S is used to visualize tubes and presence of fluid in Douglas pouch.

Advantages:

- No need of anaesthesia.
- No radiological exposure.
- Ovary is examined at same time by U/S.
- Shows tubal patency.
- Shows:
 - Uterine anomalies (septum).
 - Fibroid.

Treatment of tubal factor:

Tubal surgery is no longer recommended for severe disease since the introduction of IVF, but it still has a place in less severe cases.

(A) ART: in severe cases of pelvic adhesions.

(B) Trans-cervical cannulation of fallopian tube:

- Indication: Proximal tubal block by HSG or laparoscopy.
- Technique: Introduce a special catheter through uterine opening of tube → Selective salpingography via hysteroscope at the same time of laparoscopy.
- Value: Ensure diagnosis before treatment (50% false results BY HSG).

(C) Tubal surgery:

- Aim: To restore tubo-ovarian relationship and restore pelvic anatomy as possible.
- Approach:
 - Laparoscopic approach is the role now.
 - Conventional surgery via microsurgical technique in selected cases.
- Procedure:

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- Adhesiolysis (salpingolysis): Freeing the tube from adhesions.

- Fimbriolysis: Freeing fimbrial end from adhesions.

- Old methods:

- Salpingostomy: Artificial osteum in cases with fimbrial obstruction.

- Excision of blocked segment + End-to-End anastomosis for tubal reversal after ligation.

- Tubo-cornual anastomosis (reimplantation): In case of cornual obstruction.

- Prognosis after surgery: Pregnancy rate is 30% in properly selected cases with thin filmy bands of adhesions, but unfortunately ectopic pregnancy rate is high.

(3) Peritoneal factor

It is due to intraperitoneal adhesions:

- Post-surgical.
- Post-inflammation
- Endometriosis.

Mechanism: It interferes with the mechanism of ovum pick up by:

- Mechanical interference.
- Biochemical substances [Interleukin (IL-1), IL-6, TNF- α and prostaglandins].

It can be evaluated by laparoscopy and HSG.

Treatment: - Adhesiolysis in simple cases.

- ART in severe case.

(4) Uterine factor (5%)

Causes: hypoplasia, Asherman syndrome, submucous polyp or fibroid and refractory endometrium.

Diagnosis:

- History:

Hypoplasia: Hypomenorrhea and recurrent abortion.

Asherman syndrome: History of D&C + Amenorrhea or hypomenorrhea.

SMF: Menometrorrhagia.

- Examination: Asherman syndrome → failure of sounding.

- Investigations:

US: Hypoplasia and fibroid.

HSG: SMF and Asherman syndrome.

Hysteroscopy: SMF and Asherman syndrome.

Endometrial biopsy: Refractory endometrium.

Treatment (treatment of the cause):

- Hypoplasia: Cyclic E&P.
- Asherman: **See amenorrhea.** 3) Fibroid: Myomectomy.

(5) Cervical factor

Causes: Cervical atresia, cervicitis, cervical fibroid and hostile cervical mucus.

Investigations:

1- Quality of cervical mucus: At midcycle (estrogen effect):

- Profuse.
- Thin.
- +ve thread test (7-10 cm threading).
- +ve ferning (arborization) → presence of NaCl/KCl.

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2- Postcoital test (Sim's Huhner):

- **Idea:** Study viability of sperms in cervical mucus and vaginal fluids.
- **Precautions:**
 - No vaginal douching or intercourse for 2-3 days.
 - Semen analysis is normal.
- **Timing:**
 - Just before ovulation.
 - 4-8 hours after intercourse.

Two samples are taken from post-vaginal fornix-cervical mucus) and examined. It is considered normal if > 5 motile sperm / HPF in cervical sample.

However, a diagnosis of an adverse cervical factor does not alter the therapeutic decisions as both female factor and unexplained infertility are treated with IUI or IVF. Hence, postcoital testing is not recommended as a routine.

3- Culture and sensitivity of cervical discharge: Cervicitis.

Treatment:

Cervical stenosis: Dilatation.

Fibroid: myomectomy.

Chronic cervicitis: Cauterization + specific antibiotic.

Scanty thick mucus with clomiphene → Small dose estrogen for 5 days (starting in day 10).

Anti-sperm antibody:

- Corticosteroids and condom for 6 months.
- IUI - IVF and ET.

(6) Vaginal factor

Vaginitis: Antimicrobial.

Transverse vaginal septum: Surgical excision.

Vaginal tumors: Surgical excision.

Male factor of infertility

Causes:

Pretesticular:

Gonadotrophin deficiency: Pituitary or hypothalamic cause.

Hormonal:

- Uncontrolled DM (impotence).
- Exogenous anabolic intake.
- Hyperprolactinemia (impotence).
- Hypothyroidism.

Testicular:

Congenital: Undescended testis.

Chromosomal: Klinefelter syndrome (47xxy).

Thermal: Varicocele (controversial).

Inflammatory: Mumps/TB.

Exposure to radiation and cytotoxic drugs.

Autoimmune: Antisperm antibodies in seminal plasma.

Gonadotrophin-resistant testis.

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Post-testicular:

Bilateral obstruction of vas deferens (obstructive azoospermia):

- Congenital bilateral absent vas deferens.
- Bilateral ligation of vas during repair of hernia.
- Gonorrhea.
- Immotile cilia syndrome (Kartagener syndrome).

Failure of deposition of semen in vagina:

- Impotence.
- Retrograde ejaculation (neurologic disorders).

Diagnosis:

- (1) History.
- (2) Examination (general and local).
- (3) Investigations:

Semen analysis:

- Obtained by masturbation, coitus interruptus or spermicidal-free condom.
- Collected into sterile clean container.
- After 3-4 day abstinence.
- It is examined after $\frac{1}{2}$ -1 hour either under microscopy or by Computer-Assisted Semen Analysis (CASA).

Characters of normal semen are (WHO, 2010):

- | | |
|--|-----------------------------------|
| - Volume: > 1.5 ml. | - pH: Alkaline. |
| - Sperm count: > 15 millions/ml. | - Total: > 39 millions/ejaculate. |
| - Total motility: > 40%. | - Progressive motility: > 32%. |
| - Normal forms: > 4% (by strict criteria). | |

Characters of abnormal semen are:

- Volume:
 - **Aspermia:** No seminal fluid.
 - < 1.5 ml: Hypospermia.
 - > 7 ml: Hyperspermia.
- Count:
 - **Azoospermia:** Complete absence of sperms.
 - **Oligozoospermia:** < 15,000,000/cc.
 - **Polyzoospermia:** > 250,000,000/cc.
- Vitality and motility:
 - **Asthenozoospermia:** Weak sperm and decreased motility.
 - **Necrozoospermia:** Dead sperms.
 - **Teratozoospermia:** Increased abnormal forms.
- Increased viscosity.
- Agglutination of sperms (> 10%) suggests immunological.
- Pus cells > 5 / PHF: Pyospermia.

Doppler U/S: Varicocele.

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Laboratory studies:

- Hormonal study: Prolactin, thyroid function, FSH and LH.
- α -glucoside-oxidase enzyme (secreted by epididymis): Decrease in obstructive azoospermia.

Sperm function test.

Testicular biopsy: In case of azoospermia (failure of spermatogenesis "obstructive").

Chromosomal study: Klinefelter syndrome.

Treatment:

Medical:

- Bromocriptine \rightarrow Hyperprolactinemia.
- Thyroxine \rightarrow Hypothyroidism.
- Antibiotic \rightarrow Infection.
- Clomiphene/HMG \rightarrow Spermatogenesis.

Surgical treatment:

- Varicocele ligation.

The impact of different treatment modalities on improving fertility is controversial, and no evidence-based support for varicocelectomy.

Artificial insemination(IUI): Oligospermia and asthenospermia.

IVF or ICSI: Oligospermia and asthenospermia.

Unexplained infertility (15-30%)

Definition: Failure of conception without definite cause as shown by the routine investigations for both partners.

It may be due to:

- 1- Ovum dysfunction.
- 2- Antisperm antibody in cervical mucus.
- 3- Occult infection e.g. Chlamydia and mycoplasma.
- 4- Minimal endometriosis.
- 5- Abnormal endometrial receptivity.
- 6- Abnormal embryo development.
- 7- LUF syndrome.

Investigations:

After reviewing all previous investigations and repetition of any borderline results, laparoscopy is usually done to exclude a cause.

Treatment: Without treatment, 60% of them will conceive within 3 years.

- 1- Augmentation of ovulation and IUI.
- 2- ART if IUI fails.

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Disturbances of sexual relation

- 1- Too frequent intercourse → Immature sperms.
Too infrequent intercourse → Not coincide with time of ovulation.
- 2- Retrograde ejaculation.

Treatment: Treatment of the cause.

Intrauterine Insemination (IUI)

Indications:

1. Male causes: Failure of deposition of semen(hypospadias, impotence), oligospermia, athenospermia.
2. Female causes: Hostile cervical mucus, Severe RVF, vaginismus.
3. Unexplained infertility.

Technique of Intrauterine Insemination (IUI):

1. Controlled ovarian stimulation with Clomid or better HMG followed by HCG injection when follicle is 18-20 mm.
2. Semen preparation by swim-up technique (usually) to have the highly motile sperms in the supernatant fluid. Semen preparation gets rid of:
 - PG which causes uterine spasm and expulsion of semen.
 - Semen protein causes anaphylactic reaction.
3. Procedure is performed 34-36 hours after HCG injection. It can be repeated for 3-6 cycles (pregnancy rate = 10% / cycle).

Assisted reproductive techniques

Assisted Reproductive Techniques (ART) involve oocyte retrieval, sperm aspiration or sperm injection:

ICSI: Intracytoplasmic sperm injection.

IVF and ET: In Vitro Fertilization and Embryo Transfer.

Old methods not in current practice:

- GIFT: Gamete Intra-Fallopian Transfer; via laparoscopy
- ZIFT: Zygote Intra-Fallopian Transfer. via laparoscopy.
- SUZI: Sub-Zonal Injection of sperm.

II. Reproductive endocrinology and infertility

Intracytoplasmic sperm injection

Indications:

Male factor of infertility:

- Oligospermia, asthenospermia and teratospermia.
- Immotile sperm but still alive.
- Antisperm antibodies.
- When sperms are aspirated from epididymis or testis.

Previous failure of IVF.

Unexplained infertility.

Technique:

- Controlled ovarian stimulation by gonadotrophins. Pre-stimulation pituitary downregulation protocols using GnRH analogues or antagonist is better to avoid premature ovulation and cancellation of the cycle.
- Oocyte retrieval 34-36 hours after HCG injection (U/S-guided under general or local anaesthesia).
- Ova are incubated in culture media for 4-6 hours (for complete maturation).
- Fertilization: A single sperm is injected into cytoplasm of oocyte using micropipette under microscopy.
- Embryo transfer:
 - Fertilized ovum is transferred at 4-cell stage (after 36 hours) or sometimes blastocyst (5th day) is transferred.
 - It is placed 2 cm below uterine fundus under U/S guidance.
 - Transfer 2 embryos and the remaining are frozen or verified.

Methods of sperm retrieval in azoospermia:

MESA: Micro-insemination after Epididymal Sperm Aspiration.

TESA: Testicular Sperm Aspiration

Prognosis:

- Fertilization is 50%.
- Pregnancy rate ~ 30%.

II. Reproductive endocrinology and infertility

Polycystic ovarian syndrome (PCO)

It is a common endocrine disorder characterized by chronic oligo/anovulation and a combination of symptoms, including: menstrual disturbance, obesity, and hyperandrogenism.

Prevalence: 5-10% of women in reproductive age.

Etiology :

- Unknown, but seems to involve a complex interaction between environmental (e.g. Diet and exercise) and multiple genetic factors.
- The mode of inheritance is polygenic but more similar to an autosomal dominant pattern.

Pathogenesis:

Several factors have been implicated:

- 1) Ovarian dysfunction characterized by increased ovarian androgen production due to failure of enzyme system (aromatase enzyme) in the ovary → androstenedione accumulation which leads to:
 - Arrest of maturation of follicles (anovulation- multiple small follicles 8-12 mm).
 - ↑ androstenedione in blood → hirsutism.
 - Androstenedione → estrone (E1) in the fat → Endometrial hyperplasia.
 - E1 → hypothalamus → ↑ LH secretion
- 2) Hypothalamic dysfunction leading to ↑ LH secretion → ↑ androgen production by theca cell → estrone → hypothalamus → ↑ LH (vicious circle).
- 3) Insulin resistance: characteristic for both obese and non obese patients leading to compensatory hyperinsulinemia which acts on:
 - Liver → ↓ SHBG → ↑ free E2 which → ↓ FSH level.
 - Ovary → IGF1 stimulate theca cells → ↑ androstenedione.
 - Skin → Acanthosis nigricans.
 - ↑ Adrenal androgen production.
- 4) Leptin resistance in obese → ↑ leptin

Pathology:

Ovaries:

- Enlarged (2-3 times).
- Tunica albuginea → thickened, white, smooth.
- Multiple small sub-capsular follicles.
- Hyperplasia of theca cells due to ↑ LH.

Endometrium: Proliferative or hyperplastic "Estrogen effect".

Clinical picture:

Usually between 17- 30 y.

Anovulation:

- **Menstrual abnormalities** (80%) in the form of oligohypomenorrhea, 1ry or 2ry amenorrhea, and rarely: menorrhagia and irregular bleeding (acyclic anovular).
- **Infertility**.

Hyperandrogenism: **Hirsutism** in 60-80% of patients.



II. Reproductive endocrinology and infertility

Other manifestations:

- **Obesity:** 50% of patients.
- **Acanthosis nigricans:** grey-brown discoloration of skin of axilla, groin, under breast due to ↑ insulin.
- **Seborrhea, acne and androgenic alopecia.**

Complications:

- 1- Abnormal uterine bleeding.
- 2- Infertility.
- 3- Hirsutism.
- 4- Long term consequences:
 - Metabolic syndrome: ↑ incidence of DM, HPN, atherosclerosis.
 - Endometrial hyperplasia and carcinoma.
- 5- If pregnancy occur → ↑ abortion rate (25- 40%) and gestational diabetes.

Diagnosis:

Rotterdam's criteria for diagnosis of PCO (2003):

Presence of at least 2 of 3 of the following:

- 1- Clinical or laboratory evidence of anovulation.
- 2- Clinical/ laboratory evidence of hyperandrogenism.
- 3- Typical u/s picture of PCO.

N.B: Other causes of hyperandrogenism should be excluded.

Investigations:

U/S

- Ovarian volume > 10 cm³.
- ≥ 12 cystic follicles:
 - * arranged in periphery → neck-lace appearance.
 - * each 2-9 mm in diameter.

Hormonal profile:

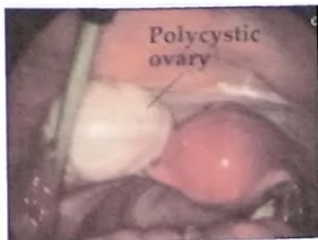
- (1) ↑ LH level and ↓ FSH level → in the 2nd day of the menstrual cycle.
- (2) ↑ LH/ FSH ratio ≥ 2: 1
- (3) ↑ Estrone (E1) due to peripheral conversion. ↓ Estradiol (E2) production by the ovary (anovulation/ arrested follicular growth) but ↑ free E2 (due to ↓ SHBG)
- (4) **Androgen:** ↑ testosterone, androstenedione, DHEA.
↑ DHEAS (adrenal origin 100%).
- (5) **High insulin level** due to insulin resistance measured by:

→ Fasting glucose: fasting insulin ratio
is < 4.5

- (6) **High prolactin level** only 30%.

Laparoscopy: Smooth whitish ovary.

Endometrial biopsy: Proliferative, hyperplastic with no secretory activity.



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D.D: Other causes of hyperandrogenism

- Cushing syndrome.
- Androgen secreting ovarian tumour.
- Androgen secreting adrenal tumour.
- Congenital adrenal hyperplasia.
- Exogenous androgen use.

Treatment:

Weight reduction:

- A small drop of weight in obese PCO patients can lead to resumption of ovulation.
- Diet modification and exercise program can achieve this goal.
- Another option in morbidly obese patients is Drugs (lipase inhibitors e.g. Orlistat) or surgery (laparoscopic gastric banding).

If pregnancy is not desired:

A. Cyclic progesterone: 10mg MPA for 10 days every 1-3 months:

- Prevents endometrial hyperplasia and carcinoma.
- Regulate cycle.

B. Combined oral contraceptive pills → the same effect.

C. TTT of hirsutism.

If pregnancy is desired:

(A) Insulin sensitizing agents:

- Metformin 500mg 1 × 3 (6- 12m)
 - it will ↓ insulin resistance, ↓ androgen.
- So they can lead to ovulation and pregnancy but not first line.
- It is better combined with clomiphene citrate.

(B) Induction of ovulation:

1- Clomiphene citrate (clomid)

If it failed add: *dexamethazone* (decreases adrenal androgen) or *metformin*.

2- Letrozole (femara) → aromatase inhibitor.

3- Gonadotropins (FSH + LH) or theoretically better pure FSH preparations in low slow regimen to avoid the high incidence of OHSS.

4- Gonadotrophin releasing hormone in pulsatile manner(not done).

(C) Surgical treatment: in resistant cases

1- Laparoscopic ovarian drilling (4 punctures via 40 watt cutting current for 4 seconds in each ovary) . It has same pregnancy rate as Gn with less risk of multiple pregnancy or OHSS.

2- Bilateral wedge resection (not done nowadays).

(D) ART "assisted reproductive technique":

If medical and surgical ttt fail .

II. Reproductive endocrinology and infertility

Hirsutism

Definition: it is excessive growth of terminal hair in abnormal site (male like pattern) → upper lip, beard, chest, upper abdomen, lower abdomen, upper back, lower back, arms, forearms, thighs & legs.

Hypertrichosis: Excessive growth of vellus (non-sexual) hair which is generalized.

Virilism: Hirsutism + defeminization (atrophy of breast) then muscularization (temporal baldness, deepening of voice, hypertrophy of clitoris, ↑ muscle mass).



Types of hair:

- 1- Terminal hair: thick, dark pigmented coarse hair (sexual hair).
- 2- Vellous hair: thin, fine, lightly pigmented hair.
- 3- Lanugo hair (fetal).

Androgen production:

| | Ovary | Adrenal | Peripheral conversion |
|---|-------|---------|-----------------------------|
| 1- Testosterone: | 25% | 25% | 50% From androstenedione |
| 2- Androstendione: | 50% | 50% | - |
| 3- Dihydroepiandrosteron: (DHEA) | 20% | 30% | 50% from DHEAS |
| 4- Dihydroepiandrosteron sulphate (DHEAS) | - | 100% | - |

Dihydrotestosterone: it is active hormone that ++ hair growth produced by 5 α reductase enzyme action on testosterone in tissues.

Androgen level:

Testosterone 20-80 ng/dl.

- 80% bound to SHBG. - 19% bound to albumin. - 1% free "biologically active".

SHBG (sex hormone binding globulin) is produced by the liver.

- Estrogens, pregnancy, hyperthyroidism → ↑ SHBG.

- Androgen, hypothyroidism, prolactin, GH, insulin, obesity → ↓ SHBG thus ↑ free testosterone.

Etiology: Hirsutism may be due to:

- ↑ androgen production ovarian-adrenal).
- ↓ sex hormone binding globulin.
- ↑ sensitivity of hair follicles.

(1) Constitutional (idiopathic):

- It is the commonest cause (90%).
- More in African, Mediterranean population.
- Positive family history.
- No menstrual abnormalities.
- It may be due to increased sensitivity of hair follicle.

(2) Ovarian cause:

- PCO "polycystic ovary" syndrome: → the commonest pathological cause.
 - ↓ conversion of androstendione to estrogen.
 - ↑ adrenal androgens.
 - Increased insulin (insulin resistance) leads to ↑ 5 α reductase.
- Stromal hyperthecosis.
- Androgen secreting tumors:
 - Sertoli-Leydig tumors.
 - Gynandroblastoma.

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- Pregnancy luteoma (maternal not fetal virilization).

(3) Adrenal cause:

- Congenital adrenal hyperplasia.
- Cushing syndrome.
- Androgen secreting tumors.

(4) Pituitary cause:

- Cushing disease: basophil adenoma.
- Acromegally \rightarrow \downarrow SHBG.
- Hyperprolactinemia \rightarrow \downarrow SHBG.

(5) Myxedema.

(6) Iatrogenic:

- Androgens.
- Progesterone (Norethisterone).
- Danazol (17 α ethinyl testosterone derivative).

(7) Obesity: It decreases SHBG.



Investigations for a case of hirsutism:

History and symptoms:

- A wide spectrum of symptoms can occur ranging from mild hirsutism, acne, and seborrhea to menstrual abnormalities while in severe cases, there is defeminization (breast atrophy) and even masculinization (clitoromegaly, harsh voice and baldness).
- Family history: familial.
- Menstrual history: oligomenorrhea- amenorrhea.
- Rate of progress (rapid with tumors).
- Presence of galactorrhea /breast atrophy.
- history of drug intake.

Examination:

- **Distribution:** The modified *Ferriman-Gallway score* is used where 9 androgen sensitive areas are given a score from 0-4 including (upper lip, chin, chest, upper and lower abdomen, upper arm, thighs, upper and lower back).... A score more than 8 indicates moderate to severe hirsutism.
- Signs of virilism.
- Acne, acanthosis nigricans.
- Breast examination (galactorrhea, atrophy).
- General feature of: Cushing, Acromegaly.
- Pelvic examination (ovarian tumor).
- Clitoral index $> 35\text{mm}^2 \rightarrow$ clitoromegaly.

Special investigations:

[1] Hormonal studies:

If there is menstrual disturbances, begin with

- 1- **Gonadotrophins:** LH/ FSH ratio $> 2/1 \rightarrow$ PCO
- 2- **Thyroid function:** TSH, T3, T4 \rightarrow hypothyroidism.
- 3- **Prolactin level:** Hyperprolactinaemia.

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If not proceed to:

1- Testosterone level:

> 200ng/ dl → adrenal or ovarian tumor.

< 200ng/ dl → exclude tumors, It may be: PCO, hyperthecosis.

Normal levels may be present in idiopathic cases.

2- DHEAS (50- 350 ug/ dl):

>700 ug/ dl → adrenal hyperplasia or tumor.

3- 24 hour urinary free cortisol or dexamethasone suppression test:

→ Cushing syndrome.

4- 17-OH progesterone level (normally < 300 ng/dl):

> 800 ng/dl → congenital adrenal hyperplasia.

[2] Imaging:

1. Ultrasonography:

- PCO.

- Tumors of adrenal or ovary.

2. CT and MRI: Adrenal-pituitary.

[3] Laparoscopy:

If there is high androgen level and no abnormality detected during imaging.

- Selective catheterization of adrenal vein/ ovarian vein → measure androgen level and confirms a tumor presence.

- Biopsy.

Treatment:

Treatment can slow further hair growth, but will not affect the already present hair which should be removed by physical methods.

Treatment of the cause:

- Weight reduction in obese patients.

- treatment of hyperprolactinemia, thyroid disease.

- Removal of tumors.

- Corticosteroids for treatment of congenital adrenal hyperplasia.

Drug therapy:

• Patients not desiring pregnancy:

1. Combined oral contraceptive pills (first line):

Action:

- ↓ LH secretion.

- Estrogen → ↑ SHBG → ↓ free testosterone.

- pills containing ethinyl estradiol plus a 3rd generation progestogens (Marvelon, Gynera, Cilest) while Yasmin contains Drospirone which is a progestagen with antiandrogen action.

2. Cyproterone acetate:

Action:

- It is a progestagen with Anti androgen effect.

- Competes with androgen at receptor level.

- Inhibits LH secretion.

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Dose: Reverse sequential manner: 100mg for 10 days (from day 5 to day 15) + Ethinyl estradiol 50 ug (day 5- day 25) → for contraception to avoid feminization of male fetus.

Side effects: If cyproterone is used alone:

- Feminization of male fetus.
- Irregular uterine bleeding.
- Nausea, vomiting and weight gain.

3. Spironolactone (aldactone):

- Compete with androgen on receptors and inhibits 5- α reductase.
- S/E are polyuria and transient hyperkalaemia.

4. Finasteride (Proscar):

- 5 alpha reductase inhibitor.
- S/E are fetal adverse effects. So, it must be combined with a proper contraception.

- Patients desiring pregnancy: induction of ovulation

Cosmetic treatment:

Permanent:

- Electrolysis.
- Photoepilation (LASER or pulsed light).

Temporary:

- Debilatory creams.
- Shaving.
- Bleaching.

II. Reproductive endocrinology and infertility

Puberty

Definition:

Puberty is the biologic transition between immature and adult reproductive function. This maturation leads to the complex development of secondary sexual characteristics involving breast, sexual hair and genitalia in addition to acceleration in growth.

Age of puberty:

There is constitutional variations, but initial pubertal changes occur between the ages of 8 and 13 years.

Physiology of puberty:

- There are many theories explaining the initiation of puberty, but the most accepted one is **release of Hypothalamic-Pituitary-Ovarian axis (HPO)**.
- Before puberty, this axis is in state of inhibition.
- Release of hypothalamic inhibition leads to GnRh secretion, increased FSH, LH formation and in turn increase in gonadal sex steroid level and ovulation.

Stages of puberty:

Thelarche: Breast budding is the first physiological sign in 90% of girls.

Pubarche (adrenarche): Pubic and axillary hair growth in response to increased androgen.

Growth spurt.

Menarche: The first menstrual period.

The HPO axis is not fully mature at time of menarche and subsequent menstrual cycles are commonly irregular.

Marshall and Tanner (1969) staging of breast and pubic hair development:

| Tanner classification | Breast | Pubic hair |
|-----------------------|---|--|
| Stage I | Prepubertal papillary elevation | Not present |
| Stage II | Breast budding | Labial hair |
| Stage III | Progressive enlargement | Hair extended to mons pubis |
| Stage IV | Areola formation, projection of areola and papilla | Lateral extension and pigmentation starts |
| Stage V | Mature; areolar recessed to general contour of the breast | Adult with horizontal upper border and spread to thigh |

II. Reproductive endocrinology and infertility

Abnormalities of puberty

(A) Precocious puberty:

Definition:

Development of breast or pubic hair in girls younger than 8 years.

Etiology: **Common aetiologies of precocious puberty:**

A- Central (GnRH-dependent):

1- **Idiopathic:** The most common cause.

2- **Organic:**

● CNS tumors:

- Hamartomas.
- Adenomas.
- CNS infection.
- Head trauma.
- Iatrogenic:
 - Radiation.
 - Chemotherapy.
 - Surgical.
- Malformations of the CNS:
 - Arachnoid or suprasellar cysts.
 - Hydrocephalus.
 - Empty sella syndrome.

B- Peripheral (GnRH-independent):

- Congenital adrenal hyperplasia.
- Testosterone/estrogen producing tumors:
 - Adrenal/ovarian carcinoma e.g. adenoma.
 - Granulosa cell tumor.
 - Leydig cell tumor.
 - Theca cell tumor.
- Gonadotrophin/HCG producing tumor:
 - Choriocarcinoma
 - Dysgerminoma.
 - Gonadoblastoma.
- Exogenous exposure to androgen or estrogen.
- McCune Albright syndrome.
- Ovarian cysts.
- Hypothyroidism.
- Aromatase excess syndrome.

1- Central precocious puberty (gonadotrophin-dependent):

- Early activation of HPO axis often termed as true precocious puberty.
- The most common cause of central precocious puberty is idiopathic; however, the central nervous system lesions must be excluded.
- **Treatment:** GnRH agonist (IM or subdermal implant). The aim of therapy focuses on preventing reduced final adult height and limiting the psychological effects of early pubertal development. Epiphyseal fusion is an estrogen-dependent process. GnRH agonist downregulates pituitary FSH and LH. So, estrogen level drops.

2- Peripheral precocious puberty (gonadotrophin-independent):

- Elevated estrogen levels may originate from a peripheral source or cyst and characterized by decreased GnRH, decreased FSH, decreased LH and increased estrogen.

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- **Treatment:** Aim to eliminate the estrogen. According to the etiology:
 - Estrogen secreting ovarian or adrenal tumor → surgical excision.
 - Hypothyroidism → thyroxine.

3- Heterosexual precocious puberty:

Androgen excess with signs of virilization is rare in childhood. It occurs due to androgen production from adrenal gland or ovary. Treatment is targeted towards the underlying etiology.

4- Partial form of precocious puberty:

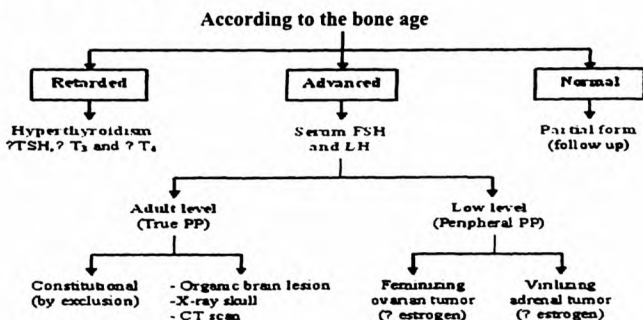
Premature thelarche, premature adrenarche and premature menarche. Each develops in isolation and without other evidence of other pubertal development.

NB: McCune Albright syndrome:

- Precocious puberty.
- Café au lait skin patches.
- Polycystic bone lesion.

Approach to a case of precocious puberty:

- 1- History and clinical examination.
- 2- Bone age study and X-ray to the lower end of radius and ulna.



(B) Delayed puberty.

Definition:

No secondary sexual characteristics are noted by age 13 years.

Etiology:

- Constitutional.
- Causes of primary amenorrhea (*see amenorrhea*).

II. Reproductive endocrinology and infertility

Menopause

Definitions:

Climacteric:

It is the transition period from reproductive capacity to non-reproductive state, when fertility and sexual activity decline. Menopausal transition is a more correct terminology.

Menopause:

It is the permanent cessation of menses as a result of ovarian follicle inactivity, it is dated by the last menstrual period that is followed by 12 months of amenorrhea. Menopause occurs naturally as a part of the climacteric.

Average age of menopause is 50 years, with a range of 43 to 55.

Premature ovarian insufficiency (premature menopause):

It refers to cessation of menses before age of 40 and is associated with increased FSH.

Pathophysiology:

- Estrogen levels decline dramatically at the menopause as a result of depletion of ovarian follicles, and the negative feedback loop is opened subsequently. GnRH is released at maximal frequency and amplitude as a result of increased FSH and LH.
- Ovarian stroma continues to produce small quantities of androstenedione and testosterone which is converted in the peripheral fat into estrone (the main postmenopausal estrogen).
- The lack of estrogen is the cause of the majority of symptoms and pathology of the menopause.

Symptoms associated with menopausal transition:

Changes in menstrual patterns:

- Shorter cycles are typical.
- Longer cycles are possible.
- Irregular bleeding, heavier, lighter with spotting.

Vasomotor symptoms:

- Hot flushes.
- Night sweats.
- Sleep disturbances.

Psychological and mental disturbances:

- Worsening PMS.
- Depression.
- Irritability.
- Mood swings.
- Loss of concentration.
- Poor memory.

Sexual dysfunction:

- Vaginal dryness.
- Decreased libido.
- Painful intercourse.

Somatic symptoms:

- Headache.
- Dizziness.
- Palpitations.
- Breast pain.
- Joint aches and back pain.

Other symptoms:

- Urinary incontinence.
- Dry, itchy skin.
- Weight gain.

Diagnosis and investigations:

The triad "hot flushes + Amenorrhea + FSH > 15 IU" makes the diagnosis easy.

D.D of menopausal symptoms:

- Depression.
- Premenstrual syndrome.
- Migraine.
- Very rarely carcinoid syndrome.

II. Reproductive endocrinology and infertility

Treatment:

General measures: Reassurance that menopause is stage of life not end of life.

Medical treatment:

(A) Non-hormonal:

- 1- **Hot flushes:** Clonidine or β -blockers can be used.
- 2- **Osteoporosis (prevention rather than treatment):**
 - Calcium 1 gm/day.
 - Calcitriol (vitamin D analogue).
 - Fluoride increases bone mass.
 - Biophosphonates decrease bone resorption.
 - SERM and tibolone (*see later*).
 - Physical activity \rightarrow Exercise program.
 - Full prevention strategies to minimize falls and prevent fractures.

(B) Hormone Replacement Therapy (HRT):

Indications:

- Treatment of vasomotor symptoms.
- Vaginal atrophy.
- Osteoporosis prevention and treatment.

The current standard of care dictates re-evaluation of the need for therapy at 6-12 month interval. HRT should be prescribed in the lowest effective dose for the shortest period of time.

Types of HRT:

1- **Estrogen replacement therapy:**

Routes of administration:

- | | | |
|-------------|------------------|--------|
| * Oral. | * Patches. | |
| * Implants. | * Vaginal rings. | * Gel. |

2- **Progestogen:**

Should be added for at least 10 days each month to reduce the risk of endometrial hyperplasia and carcinoma in a woman with autonomous.

Method of administration:

- 1- **Continuous therapy:** Amenorrhea and is suitable for postmenopausal women.
- 2- **Cyclic therapy:** 25-day estrogen and progestin is added for the final 10 days monthly and drug is withdrawn 5 days \rightarrow bleeding is suitable for women during menopausal transition.
- 3- **Tibolone:**

It is synthetic steroid that exhibits oestrogenic, progestogenic and androgenic activity.

 - * Given in a dose 2.5 mg/day to women at least one year after menopause.
 - * Results in suppression of symptoms and the prevention of bone loss.

Contraindications to HRT:

Absolute:

- | | |
|------------------------------------|-------------------------------|
| - Present or suspected pregnancy. | - Suspicion of breast cancer. |
| - Suspicion of endometrial cancer. | - Acute active liver disease. |
| - Uncontrolled hypertension. | - Confirmed VTE. |

II. Reproductive endocrinology and infertility

Relative:

- Presence of uterine fibroids.
- Past history of benign breast disease.
- Chronic stable liver disease.
- Migraine.

New developments:

(C) Selective Estrogen Receptor Modulators (SERMs):

- They do not engage the estrogen receptor in all tissues but do so selectively, with retaining the protective oestrogenic effect on the skeleton while avoiding vaginal bleeding and fear of breast cancer.
- The first SERM raloxifene is licensed for prevention and treatment of bone loss.
- Raloxifene does not reduce, indeed may exacerbate the vasomotor symptoms of menopause and so its use is restricted to patient at risk of developing osteoporosis.

(D) Phyto-estrogens:

They occur in cereals, legumes and vegetables. They are naturally occurring estrogens. They are under trial and no settled evidence of their benefits.

Premature menopause

Definition: Permanent cessation of menstruation (ovarian function) before age of 40y due to depletion of ovarian follicles or failure of follicles to respond to gonadotrophins. Also called (premature ovarian failure or hypergonadotrophic- hypogonadism).

Incidence: 1% of women < 40y.

Etiology:

- 1- Constitutional (idiopathic): in most cases no cause is found.
- 2- Chromosomal disorder:
 - Mosaic turner (46 XX / 45 XO).
- 3- Metabolic disorder: galactosemia.
- 4- Irradiation- chemotherapy.
- 5- Infection: mumps, T.B., bilateral abscess.
- 6- Autoimmune disease: anti-ovarian Ab. It is called (Blizzard syndrome; autoimmune ovarian failure).
- 7- Immunological disorder: Di George syndrome.
- 8- Resistant ovary syndrome → see amenorrhea.

Diagnosis:

- Clinically
 - amenorrhea < 40y old.
 - symptom of ↓ E → hot flushes.
- Laboratory investigations:
 - 1- ↓ estradiol level < 20 pg/ml.
 - 2- ↑ FSH level > 25 mIU/ml.
 - 3- Chromosomal study → mosaic turner.
 - 4- Ovarian biopsy (resistant ovary- autoimmune disorder).

Treatment:

HRT till the age of 50 years to decrease incidence of osteoporosis by 50- 60%.

II. Reproductive endocrinology and infertility

Sexual problems

1- Dyspareunia: "painful or difficult intercourse"

A) Primary: "Dating from first sexual intercourse".

- Infected laceration of vulva.
- Vaginismus.
- Vaginal agenesis.

B) Secondary: "present after a period of painless intercourse"

1- Superficial dyspareunia: pain at entrance of vagina.

- Vulval lesions:
 - Acute vulvitis.
 - Bartholinitis.
 - Large vulval tumor.
- Vaginal lesions:
 - Vaginitis.
 - Menopausal atrophy.
 - Large vaginal tumor.
- Extra genital cause:
 - Piles.
 - Fissure.
 - Urethral caruncle.

2- Deep dyspareunia: pain develops after penetration into vagina.

- Chronic cervicitis.
- Cervical fibroid.
- Chronic salpingitis.
- RVF "fixed".
- Pelvic endometriosis: Douglas pouch/recto-vaginal septum.
- Mass in Douglas pouch.

Treatment: Treatment of the cause.

2- Vaginismus:

Violent reflex spasm of levator ani muscle, gluteal muscles and adductors of thigh on any attempt of sexual relation or vaginal examination.

*** 1ry vaginismus: psychological**

Treatment:

- Psychotherapy.
- Sexual education.
- Gradual dilation of vagina by dilators.
- Fenton's operation.

*** 2ry vaginismus due to dyspareunia: Treatment→Treatment of the cause.**

3- Frigidity:

Absence of sexual desire or failure to achieve orgasm.

- Psychological problems.
- Endocrinal: DM, hypothyroidism.
- Female circumcision.
- Marital problems or dyspareunia.

Treatment: Psychotherapy.

- Methyl testosterone.

II. Reproductive endocrinology and infertility

Intersex

Definition: incomplete sexual differentiation either into male or female

Etiology:

1- Chromosomal intersex:

1. **Turner syndrome:** 45X0 → female

2. **Klinefelter syndrome:** 47XXY → male

- Tall

- Scanty facial hair.

- Gynecomastia (90%)

- Female hair distribution

- The penis and testicles are small: There is hyalinization of the seminiferous tubules leading to azoospermia or the production of few sperms leading to infertility.

- Some patients have more than 2 X chromosomes:

- Mental retardation increases with the increase in number of X chromosomes.

- Some have a mosaic karyotype (47 XXY -46 XY).

- The mosaic individual may be fertile.

3. **Triple x syndrome: (superfemal)**

47XXX 48 XXXX

4. **The YY syndrom:** 47 XYY 48 XYYY

Male → tall + mental retardation.

5. **Mixed gonadal dysgenesis: (45X0 / 46XY) → female.**

- Gonads: streak gonads (may be non functioning testis on one side).

- Ambiguous genitalia (patient may virilize at puberty).

- Gonadectomy is indicated to remove the source of androgens and to avoid the risk of malignancy.

2- Gonadal abnormality:

1. **True hermaphrodite:**

- Individual has ovarian & testicular tissues in different combinations:

- An ovary on one side and a testis on the other side

- An ovary or testis on one side and an ovotestis on the other side

- Ovotestis on both sides.

- The sex chromosomes may be male (XY) or female (XX) or mosaic. → (commonly XX).

- The external genital organs may be male or female or ambiguous.

- Diagnosis is made by gonadal biopsy.

2. **Pure gonadal dysgenesis:**

- Streak gonads.

- Female with infantile genital organs, primary amenorrhea, tall.

- Karyotype may be:

- 46 XX → Pure gonadal dysgenesis

- 46 XY → Swyer syndrome.

3. **Sex inversion:**

- Sex appearance is male + testis

- Chromosomal pattern 46XX

3- Hormonal disturbance:

1. **Congenital adrenal hyperplasia:**

Etiology:

- Failure of formation of cortisol from 17 α hydroxy progesterone due to:

II. Reproductive endocrinology and infertility

↓ 21- Hydroxylase enzyme (95%)

↓ 11- Beta hydroxylase enzyme

- ↓ Cortisol → ↑ ACTH → hyperplasia of adrenal gland → ↑ production of androgen.

Features:

- Virilization of female fetus (fusion of labia + enlarged clitoris + hirsutism)
- Infantile genital organ → amenorrhea.
- About 75% of infants have hyponatraemia and hyperkalaemia (salt-losing), due to decreased synthesis of aldosterone.

Treatment:

- Prednisolone or dexamethazone for life → ↓ACTH.
- Dose is adjusted by the level of 17a-hydroxyprogesterone.
- Surgical correction of external genitalia → preferably during the first 2 years of life to

avoid psychological injury of the child.

- Normal sexual and reproductive function can occur with proper medical treatment.
- Children born to a patient with CAH are examined properly as the condition is inherited as autosomal recessive disorder from the mother or father (1 in 200).

Note:

- The internal genital organs are differentiated by the tenth week of pregnancy, while the adrenal cortex does not function before the twelfth week.
- This explains the presence of fallopian tubes, uterus, and vagina. They remain infantile because of androgens secreted after twelfth week.

2. Virilization of female fetus:

- Maternal ovarian tumors → androgen.
- Mother receives progesterone or androgen.

4- Endorgan resistance: testicular feminization syndrome.

5- Psychological intersex:

- **Homosexuality:** person attracted to same sex.
- **Transvestism:** tending to wear clothes of other sex.
- **Trans-sexual:** desire to change sex

Investigations:

1- Buccal smear → bar-body

- If two X chromosomes are present, a chromatin mass or Barr body will be seen beneath the nuclear membrane of the cell, so the female cell is chromatin positive while the male cell is chromatin negative.
- The Barr body is present in 20-50 per cent of the female epithelial cells.

2- Neutrophil examination → bar-body

- The chromatin mass gives a "drum stick" appearance to one of the lobes of the nucleus.
- It is present in 20% of the neutrophils of the female subject.

3- Chromosomal analysis (karyotyping)

4- Hormonal estimation.

5- Genital organs examination by (ultrasound – laproscopy - laprotomy).

- Histological examination of the gonad is decisive.

6- CT- MRI → adrenal gland to detect tumors.

Treatment: → treatment of cause.

N.B.:

* **Pseudohermaphrodite:** gonads of one sex & genital organs of other sex.

Male pseudohermaphrodite

Female Pseudohermaphrodite.

- gonads: testis

- gonads: ovaries

- genital organs → female

- genital organs: male

II. Reproductive endocrinology and infertility

- e.g: testicular feminization syndrome

- e.g: congenital adrenal hyperplasia

* **Mosaicism:** is diagnosed if more than 5% of cells show normal karyotype.

* **The chosen sex of rearing:** is determined, then the gonadal tissue which is not appropriate to the chosen sex is removed.

III. Infections of the female genital tract

Infections of the female genital tract

Natural defense mechanisms

The following mechanisms protect the female genital organs:

- The vagina is mechanically closed by approximation of the labia and its anterior and posterior walls.
- The vagina is lined by thick stratified squamous epithelium. The reaction of the vagina is acidic.
- The cervix is closed by a mucous plug which is also bacteriolytic.
- The superficial layer of endometrium is shed every month during menstruation.

Defense mechanism is disrupted in the following conditions:

- Before puberty and after menopause. During menstruation.
- After abortion or labor.
- Broad-spectrum antibiotic therapy.
- The use of combined contraceptive pills.
- The tail of the intrauterine contraceptive device may favor the growth of bacteria.
- Vaginal douching.

Vulvitis

Etiology:

Inflammation of the vulva may be primary or secondary.

I- Primary vulvitis:

1. Skin diseases: The skin of the vulva may be affected by any primary skin disease as tinea cruris, candidiasis, furunculosis, scabies, and eczema.
2. Sexually transmitted diseases:
 - Gonorrhea. Syphilis.
 - Soft sore (Chandroid) caused by *Haemophilus ducreyi*.
 - Granuloma inguinale caused by *Calymmatobacterium granulomatis*. (Donovan bodies).
 - Lymphogranuloma venereum caused by *Chlamydia trachomatis*. Genital herpes caused by *Herpes simplex hominis virus type II*. Condylomata acuminata (genital warts) caused by HPV.
 - Molluscum contagiosum (viral infection).
3. Chronic specific diseases:
Bilharziasis. Tuberculosis. Elephantiasis. Actinomycosis.

II- Secondary vulvitis:

- The vulva may be irritated and inflamed secondary to:
1. Urinary conditions:
 - Incontinence as in urinary fistula. Pyuria.
 - Glycosuria as in diabetic cases. Severe frequency of micturition.
 2. Vaginal conditions:
 - Excessive vaginal discharge.
 - Menorrhagia and polymenorrhoea.

III. Infections of the female genital tract

3. Rectal conditions:

- Incontinence as in fecal fistula and complete perineal tear. Anal fistula.
- Oxyuris infection, particularly in children.

Diagnosis of vulvitis:

- Most cases can be diagnosed by inspection in good light.
- We must do vaginal, bimanual and speculum examination in every case. Any discharge is examined bacteriologically.
- Skin biopsy of the vulva may be needed in obscure conditions as leucoplakia.
- In suppurative conditions and in the presence of moniliasis, we have to exclude diabetes mellitus.

Treatment of vulvitis:

1. Treatment of the cause.

2. General treatment:

- Sedatives, as phenobarbitone, especially at night to prevent scratching. Antihistaminics to prevent scratching.
- In vulvitis of children and postmenopausal patients, oestrogens can be given by mouth or locally to improve the vascularity and resistance of the vulva.
- The underclothes should be of cotton (avoid nylon underwear).

3. Local treatment:

Local cleanliness: The vulva is shaved and washed several times daily with 1% sodium bicarbonate solution (soothing agent).

Antipruritic agents as cortisone, antihistaminics and anesthetic ointments.

Diabetic vulvitis

- It is the result of glycosuria which leads to chemical irritation.
- The condition is usually complicated by monilial infection because the fungus flourishes in the presence of sugar.
- The main symptom is pruritus which is exaggerated by the presence of peripheral neuritis.

Diabetic vulvitis is characterized by:

- Severe itching.
- Inflammation is widespread and may extend to the skin of the thigh. The skin is thickened and gray in colour due to scab formation.
- Furunculosis and ulcers may form as a result of scratching.

Treatment:

- Control of diabetes;
- Treatment of associated monilia infection
- General and local treatment of vulvitis as mentioned before.

III. Infections of the female genital tract

Vaginitis

Etiology:

- Inflammation of the vagina may be primary or secondary.

Primary vaginitis:

- Vulvovaginitis of children.
- Senile vaginitis.
- Trichomonas vaginitis.
- Candida (monilial) vaginitis.
- Bacterial vaginosis.
- Vaginitis emphysematosa.
- Nonspecific vaginitis.
- Cytolytic vaginitis.
- Mechanical irritation by a neglected pessary or foreign body.
- Chemical irritation due to douching with irritating medications.
- Application of radium for malignant disease of cervix or vagina
- Other types of vaginitis due to syphilis, bilharziasis, tuberculosis and diphtheria may occur.

Secondary vaginitis:

- The vagina may become irritated and inflamed secondary to:
- Urinary conditions as urinary fistula e.g. ureterovaginal and vesicovaginal fistula. Rectal conditions as rectovaginal fistula and complete perineal tear.
- Infected cervical discharge.

Bacterial Vaginosis (BV)

Definition and incidence

- Bacterial vaginosis is the most common cause of abnormal vaginal discharge in the adult woman (40-50%).
- A group of anaerobic organisms, which include *Gardnerella (G) vaginalis*, *Mycoplasma hominis*, *Ureaplasma urealyticum*, *Peptostreptococci*, *Mobiluncus* species, *Bacteroides*, and other organisms, causes infection. *G. vaginalis* is present in most cases (70-90%) but not necessarily in every case. It is a Gram-variable coccobacillus.
- These organisms replace the Döderlein bacilli which are absent or few.
- There is no inflammatory reaction and pus cells are absent and hence the term vaginosis and not vaginitis.

Mode of infection:

It is not known; however, the following are predisposing factors:

1. Sexual intercourse: It is suggested that with increased frequency of intercourse, the alkaline semen reduces the vaginal acidity allowing growth of anaerobic bacteria. It is not a sexually transmitted disease as no organism is transmitted from the husband.
2. Excessive use of alkaline vaginal douches.
3. Washing the vulva with soap (alkaline medium).

III. Infections of the female genital tract

4. The use of intrauterine device: The tail of the device may favour the growth of anaerobic bacteria.
5. A phage virus infects the lactobacilli and decreases their number allowing growth of anaerobic microorganisms.
6. Autoinfection from intestinal flora.

Symptoms:

The condition is asymptomatic in up to 50% of cases.

The only symptom is vaginal discharge, which is white or gray in color, excessive, thin, and offensive with a fishy odor. The smell may be the only noticed during intercourse. The classic discharge looks like a cup of milk which has been poured into the vagina. The offensive odor is due to the formation of amines from amino acids by enzymes (decarboxylases) produced by the anaerobic bacteria and so the condition is sometimes called anaerobic vaginosis.

There is no dyspareunia, vaginal soreness or pruritus as there is no inflammatory reaction.

Diagnosis:

Three out of 4 signs should be present for the diagnosis (Amsel's criteria):

1. White or gray, excessive, thin, and offensive vaginal discharge with a fishy odor.
2. Vaginal pH more than 4.5 (a pH below 4.5 excludes BV). Normal vaginal pH is 3.5-4.5.
3. A positive Whiff (sniff or amine) test.
4. The presence of clue cells which must form more than 20% of the exfoliated vaginal epithelial cells. They are detected by a saline wet smear or Gram stained film.

Amine (Whiff) test is performed by adding a drop of 10% potassium hydroxide (alkaline solution) to a drop of vaginal discharge on a slide. Amines are released giving a fishy odour.

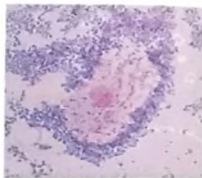
Clue cells are exfoliated vaginal epithelial cells covered with large numbers of bacteria. So, the cell borders become obscured. They appear under the microscope after adding a drop of normal saline to a drop of the vaginal discharge (wet smear). They can also be detected by a Gram-stained film. They are called "clue cells" because their presence gives a clue to the diagnosis.

Culture has no role in the diagnosis of bacterial vaginosis.

New methods of diagnosis include measuring the metabolic products of anaerobic bacteria such as aminopeptidase, and the use of DNA probes which detect the antigen of *G. vaginalis*.

Complications:

- Bacterial vaginosis in pregnancy can lead to abortion in the second trimester, chorioamnionitis, premature rupture of membranes, preterm labour, postabortive infection, and postpartum endometritis.
- In the non-pregnant patient, it causes pelvic inflammatory disease, urinary tract infection, and pelvic infection (parametritis) after hysterectomy.



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Treatment:

Metronidazole is the drug of choice. It is given in the form of oral tablets; one tablet 250 mg three times daily or one tablet 500 mg twice daily for 7 days. It can be given as 2 grams in a single dose. Metronidazole vaginal tablet (500 mg) can be inserted every night for 7 days. Also, metronidazole gel (Metrogel) can be used locally.

Clindamycin is the second choice. Oral clindamycin 300 mg twice daily for 7 days or local clindamycin in the form of a vaginal cream applied once daily for 7 days. Also, clindamycin vaginal ovule once daily for 3 days.

During pregnancy, we can give metronidazole or clindamycin.

The husband is not treated as this does not increase the cure rate or prevent recurrence of infection. The responsible organisms are not sexually transmitted.

Trichomonas vaginitis

Incidence:

It is the third most common cause of abnormal vaginal discharge in the adult woman (20%) after candidal vaginitis (30%), and bacterial vaginosis (40-50%).

Causative organism:

The *Trichomonas vaginalis* is a flagellated parasite (protozoon).

It is ovoid or pear-shaped and slightly larger than a leucocyte. It has 4 anterior flagellae, undulating membrane and a long tail.

T. vaginalis is different from *Trichomonas* found in the mouth (*T. buccalis*) and that found in the intestine (*T. hominis*).

The optimum pH for trichomonas is 5.5-6.5 i.e. weak acid medium. So, symptoms usually start immediately after menstruation as the alkaline menstrual blood reduces vaginal acidity.

Mode of infection:

1. Sexual intercourse.
2. Contamination infected towels, instruments, lavatory seats, and swimming pools.
3. Infection from the rectum may occur by organisms present in the intestinal tract. This explains infection in virgins.
4. *Trichomonas vaginalis* is present in the vagina in about 2-3% of women without producing symptoms i.e. carrier state. Change in the general or local resistance as (severe illness may change carrier state into an infected state).

Diagnosis:

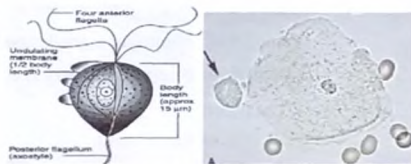
Symptoms:

Vaginal discharge: It is the main complaint. Typically, it is excessive, yellow, offensive and frothy. However, the nature of the discharge varies widely. Fotherness is due to the action of trichomonas on glycogen with production of carbon dioxide gas.

Pain and soreness of the vulva secondary to irritation by vaginal discharge.

Pruritus vulvae.

Dyspareunia due to tenderness of the vagina.



III. Infections of the female genital tract

Frequency and burning micturition if there is *Trichomonas* cystitis or irritation of urethral meatus.

Signs:

- The vulva may be inflamed, red and tender.
- The vaginal mucosa is inflamed, red and tender. Red spots may be seen especially on the portio vaginalis of the cervix and in the vaginal fornices. These spots do not bleed on touch and give the mucosa a "strawberry" or "flea-bitten" appearance which is present in less than 25% of cases.
- The cervix may be free, or it may show red spots like the vagina.

Investigations:

Fresh drop examination (wet smear): A drop of vaginal discharge is put on a slide, add a drop of normal saline (at 37°C), cover with a slip and examine at once. Under the low power magnification, the trichomonads are known by their shape, size (slightly larger than a pus cell) and rotatory movements. Many pus cells are usually present. Under high power magnification, one can observe the movement of flagellae and undulating membrane.

Stained film: The trichomonads appear dark red (Gram negative). Culture on specific media (Kupferberg or Feinberg medium).

Treatment:

CDC (2015) recommend:

- Either metronidazole 2 g once or tinidazole 2 g once,
- The husband and wife must be treated at the same time, to prevent reinfection.

The drug of choice is *metronidazole* (Flagyl). It is given in the form of oral tablets, one tablet, 250 mg three times daily or one tablet, 500 mg twice daily for seven days for both wife and husband. Metronidazole can be given as 2 grams in a single dose. Because of drug disulfiram-like effects, patients should abstain from alcohol during use and 2 hours following metronidazole therapy and or 72 hours after tinidazole. Metronidazole vaginal tablet (500 mg) can be inserted every night for 7 days. The vaginal tablets are less effective as the organisms may be found in other sites as the bladder or urethra and Bartholin glands.

The indications for local therapy are:

- Nausea and vomiting occurring with oral medication.
- Lactating women as the drug is excreted in milk.

Tinidazole can be given orally in a single dose of 2 gm for both wife and husband. At the same time, wife may use an acid vaginal douche as dilute lactic acid at night.

Coitus is avoided during treatment.

Treatment of persistent or recurrent cases:

- The cure rate of oral metronidazole is about 90%. Failure of therapy may be due to poor intestinal absorption, resistant organisms or reinfection from the untreated husband.
- In resistant cases, we double the dose and duration of therapy to be 14 days or Oral tinidazole at doses of 500 mg orally three times daily or 7 days or our times daily or 14 days have been effective in curing patients with resistant organisms.

III. Infections of the female genital tract

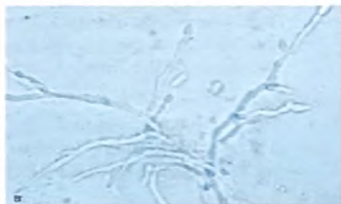
Monilial vaginitis (vulvovaginal mycosis)

Incidence:

- It is the second most common cause of vaginitis after bacterial vaginosis.
- It is oestrogen dependent infection, and so it is rare before menarche, and after menopause.

Causative organism:

- Infection is caused by a fungus called *Candida* or *Monilia*.
- There are several species as *Candida albicans*, *C. tropicalis*, and *C. glabrata*. *C. albicans* is responsible for infection in the majority of cases (90%).



Predisposing factors:

1. Presence of carbohydrate This explains why infection is common in pregnant and diabetic women.
2. High vaginal acidity: This destroys other bacteria thus allowing the fungus to flourish.
3. Broad spectrum antibiotic therapy destroys other bacteria allowing the fungus to flourish. This is the main cause of recurrent infection.
4. The use of combined contraceptive pills which increase amount of glycogen in the vaginal mucosa: estrogen also directly stimulates the growth of the fungus.
5. Corticosteroid therapy and immunosuppressive drugs.
6. Increased local moisture due to hot, moist weather or tightly fitting clothes.
7. Pregnancy because:
 - Vagina is rich in glycogen. High vaginal acidity.
 - Renal glycosuria is frequent.
 - Low immunity due to decreased T-cell activity.

Mode of infection:

- *Candida albicans* is present in the vagina of about 25% of women without producing symptoms. However, the carrier state may be changed into the infected state by the above mentioned predisposing factors.
- Contamination from infected towels, instruments, lavatory seats, and swimming pools.
- Infection from the rectum may occur by organisms present in the intestinal tract. Sexual intercourse. An infected diabetic husband with monilial urethritis or balanitis may infect his wife. This method of spread is rare.

III. Infections of the female genital tract

Diagnosis:

Symptoms:

- Vaginal discharge: Typically, it is thick, white, scanty and curdy like cottage cheese; however, the nature of discharge varies widely. It is odourless, though some patients notice the smell of yeast. An offensive discharge occurs when other bacteria are present as well.
- Pain and soreness of the vulva secondary to irritation by vaginal discharge.
- Pruritus vulvae: It is the main complaint, usually out of proportion to the amount of discharge.
- Dyspareunia due to tenderness of the vagina.
- Frequency and burning micturition due to irritation of urethral meatus.
- The symptoms are usually exacerbated during the week before menstruation, due to increased glycogen content of vaginal mucosa. Some relief occurs with the onset of the flow as menstrual blood is alkaline in reaction.

Signs:

- Both vulva and vaginal may be inflamed, red and tender.
- The discharge tends to form white patches which are adherent to the vaginal wall. Removal of these patches may cause slight bleeding.

Investigations:

- Wet smear: A drop of 10% KOH is added to a drop of discharge on a slide and examine microscopically. The fungus appears as long thin filaments (mycelia) to which small buds are attached. This alkaline solution breaks up all the cells except *Candida*.
- Vaginal pH is normal (3.5-4.5): A pH more than 4.5 excludes candidiasis.
- Stained film: Using Gram, methylene blue, or gentian violet stain. *Candida* is Gram positive and appears violet.
- Culture on specific media as Nickerson medium: Vaginal candidal culture is not routinely recommended. However, it may be warranted for those who fail empiric treatment and or women with evidence of infection yet absence of microscopic yeast. It is the best method of diagnosis; The Feinberg medium allows growth of both *Candida* and *Trichomonas vaginalis*.
- Urine analysis or fasting blood sugar must be done in every case to exclude diabetes mellitus.



Treatment:

Antifungals:

Local (imidazole drugs):

A- Clotrimazole vaginal tablets and cream: One tablet, 100 mg is inserted every night for 3 nights, or a single tablet, 1200 mg is inserted once. Cream is applied at bed time.

B- Miconazole vaginal ovules and cream: One ovule, 400 mg every night for 3 nights.

C- Ticonazole preparations.

III. Infections of the female genital tract

Oral medication:

- Itraconazole capsules. Two capsules are given and repeated after 12 hours. Fluconazole, only one capsule (150 mg) is given orally. These drugs are contraindicated during pregnancy and lactation. It is particularly indicated in unmarried females.

Alkaline vaginal douches: As 1% sodium bicarbonate solution.

Management of predisposing factors.

Vitamin B complex oral tablets: To inhibit the growth of monilia.

Recurrent vulvo-vaginal mycosis

Definition: It is defined as 4 or more attacks of candidiasis per year.

Causes:

A- Recurrence:

- Broad spectrum antibiotic therapy is the main cause of recurrent infection.
- Diabetes.
- Pregnancy.
- High-dose combined contraceptive pills. Corticosteroid therapy.
- Immunosuppressive therapy.

B- Re-infection:

- From either intestinal tract or from the husband.

C- Resistance:

- Infection with non-albicans species as *C. glabrata* and *C. tropicalis* which need longer treatment with imidazole drugs.

Treatment:

- For recurrent *C. albicans* disease,
- Treatment of any predisposing factor as control of diabetes. local intravaginal therapy for 7 to 14 days
- Induction regimen: Oral fluconazole 150 mg/3 day/3 doses (day 1, 4, and 7) are options then suppressive maintenance regimen: Oral fluconazole 150 mg/week for 6 months.
- Non-albicans candidal species are not as responsive to topical azole therapy. For nonalbicans recurrent infection, a 600-mg boric acid gelatin capsule intravaginally daily for 2 weeks has been successful. care is taken if children are in the household as accidental oral ingestion of boric acid capsules can be fatal.

Vulvovaginitis of children

Etiology:

- The commonest age is 1-5 years.
- The infection occurs because the vulva and vaginal resistance are low due to lack of estrogen and so liable to recur till puberty starts. This low resistance allows growth of pathogenic organisms, carried to the area by hands or dirty clothes.

III. Infections of the female genital tract

Causative organism:

- Any pathogenic organism as the streptococcus, staphylococcus, gonococcus, *Trichomonas vaginalis* or *Candida* may be responsible.
- Thread worms (*oxyuris vermicularis*), migrating from the rectum, may be a causative factor. Rarely, the condition is diphteric.

Mode of infection:

- Organisms are transmitted from a child or adult by hands or clothes.
- Sometimes, a foreign body as pin is inserted by the child into the vagina causing infection.
- Wiping of the perineum from anus to vagina may transfer enteric organisms, *Trichomonas vaginalis*, and *Candida* to the vagina.
- A child with otitis media or tonsillitis may transmit bacteria by hand to the vulvovaginal area.
- Sexual abuse leading to any sexually transmitted disease as gonorrhoea and *Trichomonas vaginitis*.
- Local irritants may inflame the vulva tissues as nylon underclothes.

Diagnosis:

Symptoms:

- Purulent vaginal discharge: It may be blood stained if there is a foreign body, a cervical polyp, bilharzial papillomata, or the rare sarcoma botryoides.
- Pain and soreness of the vulva secondary to irritation by vaginal discharge.
- Pruritus vulvae.
- Frequency and burning micturition due to irritation of the urethral meatus.

Signs

- The vulva is inflamed, red, tender, sometimes edematous or excoriated, and bathed in discharge. The labia minora may stick together, but can be easily separated apart leaving inflamed red surfaces.

III- Investigations

- The discharge is examined by wet smear, Gram stained film, culture and sensitivity test.
- The presence of a foreign body can be excluded by rectal examination, X-ray examination, sonography, or examination under general anaesthesia using a nasal speculum, a baby laryngoscope, a vaginoscope, or urethroscope.
- Recurrent cases need stool examination for thread worms.

Treatment:

- A specific antibiotic is given according to the nature of the organism.
- In nonspecific vaginitis, an oestrogen cream is applied to the vulva each night for about 2 weeks. It increases local resistance to infection and relieves soreness.
- Any foreign body must be removed.
- Sedatives as phenobarbitone especially at night to prevent scratching.
- Local washes with warm water and if the vulva is excoriated the child is kept at rest and adhesion of the labia is prevented by application of zinc oxide cream.
- Boiling of the underclothes which should be of cotton. Isolation from other children to prevent cross infection.

III. Infections of the female genital tract

Senile (atrophic) vaginitis

Etiology:

- After menopause (natural or artificial), the vaginal epithelium becomes thin and atrophic and the vaginal acidity is lowered, pH becomes 6-8. This is due to deficiency of oestrogen.
- These factors predispose to vaginitis by allowing growth of organisms which are normally inhibited by the protective mechanism. Senile endometritis is sometimes present as well.

Diagnosis:

Symptoms:

- A postmenopausal purulent, sometimes blood stained vaginal discharge.
- Pain and soreness of the vulva secondary to irritation by vaginal discharge. Pruritus vulvae may be present.
- Dyspareunia due to tenderness of the vagina.
- Frequency and burning micturition due to irritation of the urethral meatus.

Signs:

- The vulva may be inflamed, red and tender.
- The vaginal mucosa is thin, atrophic with absent rugae. It shows areas of ulceration which appear as bright red spots that bleed on touch. The raw areas may become adherent forming adhesions (adhesive vaginitis).

Treatment:

- Estrogen is given orally or locally to increase vaginal resistance. Acid vaginal douches as dilute acetic acid once or twice daily.
- In resistant cases, the uterus is curetted to exclude carcinoma of uterus or associated senile endometritis. Antibiotics are not used to treat senile vaginitis.

Nonspecific vaginitis

- It is vaginal inflammation in absence of a specific organism as the gonococcus or Trichomonas. It is due to organisms as streptococci, staphylococci, and E. coli.
- This can occur before puberty or after menopause as the vaginal acidity is low and the vaginal epithelium is thin and can be infected by nonspecific bacteria.
- Nonspecific vaginitis of children and postmenopausal patients is best treated with local oestrogen.

Vaginitis emphysematosa

- It is a rare condition, mostly seen in pregnant women.
- There are numerous small bullae in the vaginal epithelium which are filled with carbon dioxide gas. The surrounding tissues are hard and indurated and there is excessive purulent discharge.
- True cause is unknown, but may be due to Trichomonas or Gardenerella vaginalis. It is treated with metronidazole.

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Cytolytic vaginitis

Causative organism:

- Overproduction of Döderlein bacilli is responsible for the condition.
- Some species of these bacilli produce hydrogen peroxide which causes vaginal irritation and cytolysis of vaginal cells.

Diagnosis:

Symptoms:

- Vaginal discharge which is white or paste-like.
- Pain and soreness of vulva secondary to irritation by vaginal discharge. Pruritus vulvae.
- Dyspareunia.
- Frequency and burning micturition.

Investigations:

- Wet smear: Increased Döderlein bacilli and the vaginal cells show cytolysis.
- Vaginal pH is less than 4.5.

Treatment:

- Alkaline vaginal douches using sodium bicarbonate (30-60 gm/litre) 2 or 3 times per week and continued till symptoms disappear.

Cervicitis

Acute cervicitis:

Etiology:

- Gonorrhoea.
- Chlamydial infection.
- Puerperal infection after abortion or labour. Cauterization of cervix.
- Postoperative e.g. after dilatation of cervix.



Symptoms:

- Mucopurulent vaginal discharge. Pelvic pain and low backache.
- Dyspareunia.

Signs:

- The cervix is swollen and deep red in colour (angry looking cervix). A mucopurulent discharge exudes from the external os.
- Marked tenderness occurs if the cervix is moved from side-to-side.

Treatment:

- Antibiotics are given.
- Any local treatment is contraindicated to prevent ascent of infection.

Prognosis:

- If acute cervicitis is not properly treated, it tends to become chronic because:
- The endocervical mucosa is thrown into rugae and this interferes with drainage of infection.
- The cervical mucosa does not shed during menstruation.

III. Infections of the female genital tract

Chronic cervicitis:

Etiology:

- It is a common gynaecological lesion. It is the result of acute cervicitis or it is due to a mild infection from the start.

Causative organisms:

- Gonococci, Chlamydia trachomatis, and nonspecific organisms as streptococci, staphylococci, and Escherichia coli are common.
- Tuberculosis, bilharziasis, and syphilis are rare causes of chronic cervicitis.

Symptoms:

- The condition may be asymptomatic. However, the patient may complain of one or more of the following:
- Vaginal discharge: It is mucoid or mucopurulent, and sometimes blood stained (the mucus is due to overactivity of the secretory cells of the cervical canal).
- Contact bleeding is liable to occur with vascular erosion or mucous polypi (bleeding during intercourse, vaginal examination or douching).
- Soreness and pruritus vulvae due to irritation of vulva by discharge.
- Low backache (sacralgia), due to spread of infection along the uterosacral ligaments.
- Pain in the lower abdomen or iliac fossa, due to spread of infection causing chronic parametritis.
- Dyspareunia if infection has caused parametritis. Pain is produced when the cervix is moved laterally.
- Symptoms of pelvic congestion as congestive dysmenorrhoea and menorrhagia. Infertility: Cervicitis destroys the secretory cells of the endocervix making the cervical mucus scanty and thick preventing the ascent of spermatozoa. Also, pus cells affect sperm motility and migration.
- Frequent and burning micturition: Infection may spread to the bladder by lymphatics causing cystitis.
- Rheumatic pains and allergic manifestations because chronic cervicitis acts as a septic focus.

Signs: The cervix will show one or more of the following lesions:

Chronic endocervicitis: The cervix looks more or less normal, but there is a mucopurulent discharge escaping from the external os because infection is limited to the mucous membrane of the cervical canal.

Cervical erosion (ectopy): This appears as a bright red area around the external os.

Mucous polypi of the cervix: These appear as one or more soft, bright or dark red swellings projecting from the external os. The polyp has a pedicle arising from the endocervix. Infection causes hyperplasia of the endocervical epithelium and polyp formation. The polyp may bleed on touch.



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Chronic hypertrophic cervicitis: The cervix is enlarged, congested and firm in consistency due to excessive fibrosis. It is due to longstanding infection of the cervix or chronic congestion as in case of prolapse.

Ectropion: If the cervix is bilaterally torn, the anterior and posterior lips become everted, thus exposing the endocervix.

Nabothian follicles or cysts: The openings of cervical glands (crypts) become obstructed by plugs of mucus, pus, epithelial cells or fibrosis. The glands become distended with secretion forming follicles or cysts. They appear blue if they contain mucus, or yellow if they contain pus.

Investigations:

- Bacteriological study of the cervical discharge by culture to exclude specific organisms as Gonococci and Chlamydia.
- Cervical smear or colposcopic examination to exclude malignancy.

Complications:

- Ascending infection as salpingitis: This is liable to occur after abortion, labour or hysterosalpingography.
- Cystitis due to spread of infection by lymphatics. Infertility.
- Rheumatic pains and allergic manifestations due to the presence of a septic focus.

Note: Chronic cervicitis, cervical erosion and lacerations are no longer considered aetiological factors in cervical carcinoma.

Treatment:

- Medical treatment:

Vaginal douches and insertion of antiseptic vaginal tablets. This treatment gives temporary relief, it is not curative because infection is deep seated in the cervical canal and cannot be reached by drugs applied locally.

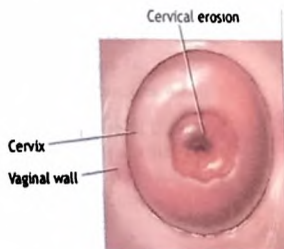
Except in case of gonorrhoea and chlamydial infection, systemic antibiotics are useless because an active infection is not present.

- Cauterization: In patients for whom the culture is not positive and empiric treatment course of antibiotics fails to cure the case, cauterization can be used by cryo or laser or electrocautery.
- Trachelorrhaphy: Infected cervical lacerations are excised and the cervix is reconstructed by a plastic operation.

Cervical erosion (ectopy)

Definition:

- It is an area around the external os of the cervix covered by columnar epithelium instead of the squamous epithelium, which normally covers the portio vaginalis.
- It is bright red in colour because the columnar epithelium is thin and shows the colour of the blood in the underlying blood vessels.



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Etiology:

- 1) Congenital erosion: Due to persistence of the condition found during the intrauterine life where the columnar epithelium of the cervical canal covers a variable area of the portio vaginalis around the external os. Normally, at full term, the portio vaginalis of the cervix becomes completely covered by squamous epithelium except in about one-third of cases when it remains covered by columnar epithelium giving rise to congenital erosion.
- 2) Hormonal erosion. This is caused by a relative excess of oestrogen. This hormonal imbalance stimulates the columnar epithelium to grow at the expense of the squamous epithelium. This explains why erosion is frequent during pregnancy and in patients taking contraceptive tablets (pill ectopy). The lesion disappears 3-6 months after delivery.
- 3) Infective erosion as a result of chronic cervicitis

Types of erosion:

- 1) Simple or flat erosion: The columnar epithelium forms a flat layer around the external os.
- 2) Papillary erosion: The columnar epithelium grows in the form of papillae which are raised on the surface. The surface of the erosion becomes irregular and gives a velvety feeling on touch.
- 3) Follicular or cystic erosion: The openings of the cervical glands become obstructed by plugs of mucus, pus, epithelial cells or fibrosis. The glands become distended with secretion forming Nabothian follicles or cysts which appear under the columnar epithelium of erosion. They appear blue if they contain mucus, or yellow if they contain pus.

Clinical picture:

Symptoms: As chronic cervicitis.

Signs:

- A papillary erosion gives a velvety feeling on touch. A vascular erosion gives contact bleeding on touch.
- Speculum examination shows a bright red area around the external os.

Investigations:

- Cervical smear or colposcopic examination to exclude malignancy.

Treatment:

- Congenital or nulliparous erosion is usually not infected and requires no treatment. Postpartum erosion is left for 3 months as spontaneous cure may occur.
- Asymptomatic erosion does not require treatment.
- When symptoms are present, treatment is by cauterization.

Cauterization of the cervix

Aim and indications:

- Cauterization destroys infected tissues, and surrounding healthy tissues grow to cover the raw area.

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- Cauterization is used in cases of chronic cervicitis, symptomatic cervical erosion and some cases of cervical intraepithelial neoplasia.

Precautions:

- A cervical smear is taken or the cervix is examined by the colposcope before cautery to exclude malignancy.

Types:

- It may be electric cautery, diathermy cautery, cryocautery, laser cautery, or cold coagulation.

Electric or diathermy cauterization:

- It is done few days after menstruation to give a chance for healing to occur before the next period.
- It is done without anaesthesia because the cervix is not sensitive to heat but sensitive only to dilatation. However, in a nullipara it is preferable to dilate the cervix up to 5 mm (No. 5 Hegar dilator) under general anaesthesia before cauterization.
- The electrode is used to cauterize the anterior wall of the cervical canal extending from just below the internal os downwards to the external os.
- The posterior wall is then cauterized.
- The lateral walls are not cauterized to avoid the cervical branch of the uterine artery.
- The whole area of erosion on the portio vaginalis is also cauterized.
- Nabothian follicles are punctured and their lining destroyed by cautery. No douching and no sexual intercourse for 2-3 weeks.

Complications of cauterization:

- Ascending infection as salpingitis and parametritis.
- Secondary haemorrhage
 - May occur 7-10 days after cautery
 - Due to separation of the necrotic tissue.
- Vaginal discharge which gradually disappears within 6 weeks, when the cauterized area becomes covered with stratified squamous epithelium.
- Fibrosis and cervical stenosis and this
 - May lead to dysmenorrhoea, hematometra, infertility or cervical dystocia during labor.
 - Avoided by proper technique and passing a uterine sound after healing is complete.

Cryocautery:

- Cautery by deep freeze may be used, it allows better healing and complications as haemorrhage, infection and fibrosis are less. However, it causes a profuse vaginal discharge for 2-3 weeks postoperatively.
- Carbon dioxide, nitrous oxide or nitrogen-all in liquid state-are passed through a hollow probe placed in the cervical canal and against the external os. Freezing (-60°C) is allowed for 2-4 minutes but not more.

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Laser cautery:

Laser beam is used to destroy infected tissues.

Complications as haemorrhage, infection and fibrosis are less and with rapid healing. However, it is costly and needs experience.

Cold coagulation:

Using Semm cold coagulator, the technique destroys tissues by heat. However, the temperature reaches only 100°C.

Cold coagulation is a misnomer as it is cold relative to the high temperature of electrocautery.

Pelvic Inflammatory Disease

Definition:

- Pelvic Inflammatory Disease (PID) means infection of the upper genital tract i.e. infection of the uterus, fallopian tubes, ovaries, as well as the parametrium, and pelvic peritoneum.
- When the term is used, it does not indicate the actual site of infection but simply indicates infection affecting any part of the upper genital tract. However, if the site of infection could be determined by laparoscopy, laparotomy or endometrial biopsy then the anatomical site of infection is mentioned as endometritis, salpingitis, etc....
- Frequently, PID is used to describe salpingo-oophoritis.
- Infection of the tube is usually bilateral and usually associated with involvement of the ovaries. Infection may be acute or chronic.



Etiology:

Causative organisms:

- Chlamydia trachomatis (40-50%). Gonococci.(25%)
- Streptococci and staphylococci: Following abortion or labour.
- Escherichia (E.) coli from adherent bowel as in case of appendicitis, and diverticulitis.
- Mycoplasma species: M. hominis, M. genitalium, and Ureaplasma urealyticum.
- Anaerobic organisms e.g. bacteroides and Clostridium species.
- Tubercle bacilli.
- Schistosoma haematobium.
- Actinomycetes: These may cause infection in the presence of intrauterine contraceptive device.
- Other organisms as pneumococci and typhoid bacilli.

Note: Acute infection is by a single organism mostly Chlamydia. Chronic infection is polymicrobial.

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Routes of infection:

- **Ascending infection:** It is the commonest method (99%). In gonococcal and chlamydial infection, the organisms pass upwards along the lumen of uterus and tubes. In cases of abortion or labour, the streptococci and staphylococci pass along the parametrial lymphatics and veins. Ascending infection may occur after hysterosalpingography, dilatation and curettage or due to the presence of an intrauterine contraceptive device.
- **Spread from an adherent infected organ** as in case of appendicitis or diverticulitis. **Bloodborne infection** as in case of tuberculosis, bilharziasis and tonsillitis.

Predisposing factors:

- Excessive sexual activity especially with multiple partners.
- Postpartum or postabortive endometritis or cervical lacerations. Genital manipulations as HSG, D.C, hysteroscopy.
- IUCDs (oral contraceptive pills, barrier contraceptives, tubal ligation and pregnancy are all protective measures).

Prophylactic measures:

- Full aseptic techniques in abortion, labour and vaginal operations.
- IUCD should be inserted under full aseptic technique with proper patient selection. Exclusion of chronic cervical infection before vaginal manipulations.
- Proper treatment of lower genital tract infections.

Acute salpingitis

Pathology:

According to the site of infection:

- **Acute endosalpingitis:** Infection starts in the mucosa.
- **Acute interstitial salpingitis:** Infection starts in the muscle wall.
- **Acute perisalpingitis:** It may occur after abortion or labour.

According to the degree of severity:

- **Acute catarrhal salpingitis:** Infection is mild and resistance of the patient is high. Infection is limited to the mucous membrane which becomes congested, red and oedematous. The lumen contains serous exudates. It usually undergoes complete resolution or forms a hydrosalpinx.
- **Acute suppurative salpingitis:** Infection is severe and involves all the layers of the tube which become infiltrated with polymorphs. The lumen contains a purulent exudate. It may lead to the formation of a pyosalpinx. Gangrenous infection never occurs because the tube has a double blood supply (uterine and ovarian arteries).

Complications:

Early complications:

- Peritonitis (generalized or localized) and pelvic abscess. Pelvic cellulitis and thrombophlebitis.
- Tubo-ovarian abscess.
- Septicaemia and septic shock.

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- Fitz Hugh Curtis (perihepatitis) syndrome.

Late complications:

- Chorionicity and recurrent attacks.
- Infertility due to tubal damage.
- Increased risk of ectopic pregnancy.
- Pelvic adhesions leading to dyspareunia and chronic pelvic pain. Intestinal adhesions and intestinal obstruction.

Diagnosis:

History:

- There may be a history of recent abortion, labour, gonococcal infection or operation as curettage or hysterosalpingography.

Symptoms:

- General symptoms of infection in the form of fever, rigors, and nausea with or without vomiting.
- Severe lower abdominal pain bilateral in nature, but rarely bilateral. Mucopurulent vaginal discharge if there is associated cervicitis.
- Dysuria and frequency of micturition.

Signs:

I- *General examination*: There is fever (38°C and above) and rapid pulse.

II- *Abdominal examination*:

- Bilateral lower abdominal tenderness and rigidity.
- Maximal tenderness is at the tubal points (half an inch above the middle of the inguinal ligament).

III- *Vaginal examination*:

- Speculum examination to take 3 swabs: one from the cervical canal to detect Chlamydia; another one from the cervical canal to detect Gonococci; the third one from the posterior vaginal fornix for aerobic and anaerobic bacteria. The specimens are examined by microscopy, and culture and sensitivity test.
- On bimanual examination, the lateral vaginal fornices are very tender and pain is produced when the cervix is moved from side-to-side. It is often difficult to feel the uterus and adnexa because of tenderness and rigidity. Pelvic abscess is felt as tender mass in pouch of Douglas.

Investigations:

IV- *Laboratory investigations*:

- Examination of cervical and vaginal swabs as mentioned above. Blood picture shows leucocytosis in 50% of cases.
- C-reactive protein may be raised (in 80%).
- Urine analysis to exclude cystitis and pyelonephritis.

V- *Ultrasonography*: To diagnose adnexal or pelvic mass.

VI- *Laparoscopy*:

- It is done if the cause of pain is not clear (it is the most accurate way to diagnose salpingitis). It is also done if the patient is not responding to treatment. Also done in case of recurrent pelvic pain.
- The diagnostic laparoscopic criteria of acute salpingitis include erythema and/or oedema of the fallopian tube, exudate from the fimbrial end, fluid in

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Douglas pouch, fimbrial agglutination, pyogenic membrane on the serosa, and presence of inflammatory masses.

Clinical criteria for diagnosis:

I- *Major criteria (all must be present):*

- Lower abdominal pain and/or tenderness. Adnexal tenderness.
- Cervical motion tenderness.

II- *Minor criteria (one of these must be present):*

- Fever ($\geq 38^{\circ}\text{C}$).
- Abnormal vaginal or cervical discharge.
- Fluid in the pouch of Douglas or pelvic abscess. Leucocytosis and elevated sedimentation rate. Elevated C- reactive protein.
- Infections with Chlamydia or Gonococci documented by cultures.

III- *Sure criteria:*

- Laparoscopic evidences of acute PID.
- Tubo-ovarian abscess on sonography or other pelvic imagings.
- Histopathological evidence of endometritis in endometrial biopsy.

Staging of acute PID (Gainesville staging):

- Stage I: Acute PID without peritonitis
- Stage II: Acute PID with peritonitis
- Stage III: Acute PID with tubo-ovarian abscess or tubal occlusion
- Stage IV: Acute PID with ruptured tubo-ovarian abscess
- Stage V: Acute PID with respiratory complications as ARDS

Differential diagnosis:

- Subacute disturbed ectopic pregnancy (missed period, absent fever, pain is unilateral, vaginal bleeding, fainting and unilateral tender adnexal mass).
- Acute appendicitis (maximum tenderness at McBurney point).
- Cystitis and pyelonephritis (loin pain, tender renal angle and pyuria). Other causes of acute abdomen as complicated ovarian cyst.

Treatment:

General measures:

- Admission to hospital is indicated in:
- Severe illness (stages II, III, IV and V). Nullipara or patient of low parity as reproductive function is of concern.
- Suspected associated pregnancy.
- Unsure diagnosis.
 - Complete rest in bed in semisitting position. Light diet and excessive fluids.
 - Relief of pain by application of heat to the lower abdomen by a thermopad. Analgesics are given if diagnosis is definite.

Antibiotics:

- Immediate and vigorous treatment with antibiotic therapy should be started without waiting the results of cultures.

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Inpatient management:

- A combination of drugs is given to act against Gonococci, Chlamydia, aerobic and anaerobic bacteria:
- Regimen I (Ceftriaxone I.V + Doxycycline I.V) followed by oral Doxycycline + Metronidazole for 14 day.
- Regimen II (Clindamycin + Gentamycin) followed by oral Doxycycline + Metronidazole for 14 day..

Parenteral antibiotics should continue until the patient has been afebrile for 48 hours e.g. gentamycin and clindamycin are given intravenously for at least 4 days followed by oral clindamycin for 10-14 days.

Outpatient management:

- 1- We can give Ciprofloxacin 500 mg orally twice daily plus Metronidazole 500 mg orally twice daily for 14 days. Ciprofloxacin acts against both Chlamydia and Gonococci.
- 2- I.M Ceftriaxone 250 mg once followed by oral Doxycycline and Metronidazole for 14 day.

Surgical treatment

Indications:

- Pelvic abscess.
- Tubo- ovarian abscess.
- Rupture of a tubo-ovarian abscess.
- Severe disease or spreading of peritonitis refractory to medical treatment.

Operations:

- In case of pelvic abscess, the posterior vaginal fornix is incised (posterior colpotomy) and drainage is maintained by inserting a rubber tube.
- Ultrasound guided or laparoscopic aspiration of tubo-ovarian abscess.
- Laparotomy, drainage and unilateral adnexectomy if preservation of infertility is necessary
- Laparotomy, drainage and TAH+BSO if preservation of infertility is not necessary.

Chronic salpingitis

Etiology:

- It is always preceded by acute or subacute salpingitis except in certain conditions as tuberculosis and bilharziasis when infection is chronic from the start.

Pathology:

Hydrosalpinx:

- It is the result of catarrhal salpingitis.
- The fimbrial end of the tube is closed by adhesions and the tube becomes distended with clear serous fluid forming a retort-shaped swelling.



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- The interstitial part of the tube remains patent, hence hydrosalpinx can be diagnosed by hysterosalpingography.
- It rarely exceeds the size of an orange.
- Peritubal adhesions are absent or minimal so a hydrosalpinx can undergo torsion.
- In some cases, the fluid of a hydrosalpinx escapes from its uterine end leading to intermittent escape of serous discharge from the vagina. This condition is known as intermittent hydrosalpinx (hydrops tubae profluens). The discharge of fluid into the uterine cavity may prevent implantation of the embryo after In Vitro Fertilization (in 50%), and it is recommended to perform salpingectomy before the procedure to improve the results.

Pyosalpinx:

- It is the result of suppurative salpingitis or secondary infection of a hydrosalpinx. It is retort-shaped.
- The tubal wall is thick fibrous and infiltrated with inflammatory cells. Because the wall is thick, a pyosalpinx does not reach a large size.
- The tube is surrounded by dense adhesions "and so the uterus may become fixed in retroversion.

Chronic interstitial salpingitis:

- Infection affects mainly the muscle layer.
- The wall of the tube is thick, fibrous and may show interstitial abscesses. The lumen becomes stenosed and this predisposes to tubal pregnancy.

Salpingitis isthmica nodosa:

- This condition consists of one or more outpouchings or diverticula of tubal epithelium in the isthmic region.
- The lesion is bilateral in 80% of cases. Microscopically the nodule consists of hypertrophied muscle containing gland spaces lined by tubal epithelium.
- The true cause is unknown but most probably it is a postinflammatory lesion or adenomyosis-like process.

Tubo-ovarian cyst: A hydrosalpinx communicating with a follicular cyst of the ovary.

Tubo-ovarian abscess: A pyosalpinx communicating with an ovarian abscess.

Perisalpingitis:

- Active infection disappears leaving the tube surrounded by adhesions.
- These adhesions may cause kinking of the tube, fixed retroversion or chronic intestinal obstruction.

Chronic specific salpingitis: Due to tuberculosis, bilharziasis or actinomycosis.

Diagnosis:

Symptoms:

- A continuous dull aching lower abdominal pain and backache.
- Symptoms of pelvic congestion in the form of congestive dysmenorrhoea, menorrhagia, polymenorrhoea and increased normal vaginal discharge (leucorrhoea).

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- Dyspareunia due to the presence of inflamed tender swellings in Douglas pouch. Dysuria and dyschezia if extensive adhesions have formed in the pelvis.
- Infertility, as a result of tubal obstruction. It is sometimes the only complaint. General ill-health and rheumatic pains due to the presence of a septic focus. Recurrent attacks of acute salpingitis.

Signs:

General examination: In case of pyosalpinx, patient may look ill and anaemic.

Abdominal examination: Tenderness may be detected over lower abdomen.

Vaginal examination:

- The uterus may be fixed in retroversion.
- In case of hydrosalpinx and pyosalpinx, an elongated cystic swelling is felt in the region of the adnexa. It is usually tender and bilateral.
- In chronic interstitial salpingitis, the tubes are thickened and tender.
- In extensive cases, the whole pelvis is filled with a tender indurated mass from which the pelvic organs cannot be differentiated (frozen pelvis).
- Sometimes, pelvic examination does not show any abnormality as in case of perisalpingitis with peritubal adhesions.

Investigations:

- Complete blood count to show leucocytosis if there is a superimposed active infection;
- Sonography to diagnose adnexal or pelvic mass; CT scan or MRI to diagnose small masses;
- Laparoscopy as a diagnostic aid in case of chronic pelvic pain.

Differential diagnosis:

- Pelvic endometriosis.
- Tuberculosis of pelvic organs. Uterine fibromyomata.
- Ovarian and broad ligament tumor. Chronic appendicitis. Diverticulitis.

Complications:

Infertility.

Increased risk of ectopic pregnancy. chronic pelvic pain.

Torsion and haematosalpinx of hydrosalpinx leading to acute abdomen. Rupture of hydrosalpinx due to trauma, e.g. bimanual examination.

Pelvic adhesions leading to intestinal obstruction and fixed RVF.

Rupture of pyosalpinx leading to septic peritonitis and pelvic abscess. Tubal fistula, a pyosalpinx may open into the bladder or vagina.

Recurrent attacks of acute salpingitis.

Chronic ill-health and rheumatic pains because it acts as a septic focus.

Treatment:

Medical treatment:

Local heat in the form of short-wave therapy.

Pelvic decongestants (Glycerine ichthyol vaginal pessaries). Analgesics for pain.

Antibiotics: where possible, any infective agents should be identified and treated (e.g. TB).

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Surgical treatment:

Indications:

Failure of medical treatment to relieve symptoms as pelvic pain. Recurrent attacks of acute salpingitis.

Large tubal swelling. Infertility.

Types of operations:

1. Salpingectomy: Removal of the affected tube with or without the corresponding ovary.
2. Hysterectomy and bilateral salpingo-oophorectomy is the treatment of choice in women above the age of 40 if both tubes and ovaries are affected.

Management of chronic PID with infertility:

1. **Adhesiolysis and tubal surgery:**

In case of infertility, the aim of operation is to restore tubal patency by:

- i- Salpingolysis (adhesiolysis) to free the tubes from adhesions.
- ii- Fimbrioplasty (lysis of perifimbrial adhesion and dilatation of fimbrial phymosis).

2. **ART:**

- It is indicated when tubal obstruction cannot be corrected by surgery and when surgery fails.
- Salpingectomy or drainage of any tubal collection can be done to improve the results of ART.

Vaginal discharge

Definitions:

Leucorrhea means the flow of a white substance and it is used to indicate an increased amount of the normal vaginal discharge.

Sometimes, the term is used to indicate all abnormal vaginal discharges except blood.

The normal vaginal discharge:

- Normally, the vulva and vagina are kept moist by a discharge derived from the following sources:
- **Vulva:** The Bartholin glands secrete alkaline mucus during sexual stimulation. Secretion from Skene tubules contributes to lubrication of the vulva.
- **Vagina:** It contains no glands but it is kept moist by a serous transudate from their wall which is acidic in reaction due to the presence of lactic acid (pH 3.5-4.5).
- **Cervix:** The endocervix secretes alkaline mucous discharge (pH 8.5) which plugs the cervical canal and prevents ascent of infection. Oestrogen increases the amount and fluidity of cervical secretion.
- **Endometrium:** It secretes an alkaline fluid rich in glycogen, glucose and fructose during the secretory phase of the cycle (uterine milk).
- The tubes secrete a serous fluid rich in proteins reaching the vagina at times.

Etiology of vaginal discharge:

- Physiological discharge:
- Increased normal discharge (true leucorrhoea) occurs in the following conditions:

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- At puberty due to increased vascularity of genital organs and unopposed oestrogenic stimulation. The increased discharge may occur a few years before or after menarche and it is temporary and corrects itself.
- At ovulation due to increased cervical secretion (effect of oestrogen).
- Premenstrual due to pelvic congestion and increased secretion of endometrial glands.
- Postmenstrual from the healing endometrial surface.
- Pregnancy because of hyperaemia and hyperestrinism.
- Pelvic congestion due to any cause as constipation and retroversion. Sexual excitement due to Bartholin gland secretion.
- Hormonal non-infected cervical erosion because the columnar epithelium of the erosion secretes mucus.
- Vaginal adenomatosis. Columnar epithelium replaces the squamous lining of the vagina. This epithelium is cervical in type and secretes mucus.
- The estrogen- progestogen contraceptive tablet.
 - Pathological discharge:
- 1. Lesions in the vagina:
 - All types of vaginitis, especially due to Monilia, Trichomonas, and bacterial vaginosis.
 - Ulcers of the vagina which may be traumatic, chemical, inflammatory, neoplastic and post-irradiation.
 - Tumours of the vagina.
 - Retained foreign body or neglected pessary.
 - Abnormal communications with the vagina as vesicovaginal and rectovaginal and rectovaginal fistulae.
- 2. Lesions in the cervix:
 - Cervicitis and infected erosion. Ulcers of the cervix.
 - Tumors and polypi of the cervix.
- 3. Uterine causes:
 - Endometritis (puerperal, tuberculous, bilharzial and senile), benign and malignant tumours and intrauterine contraceptive device.
- 4. Tubal causes:
 - Intermittent hydrosalpinx. Tumours.

Investigation of a case of vaginal discharge:

- History:
 - Age: The commonest causes of vaginal discharge in children are vulvovaginitis, foreign body and oxyuris infection. The commonest causes in adult life are bacterial vaginosis, monilial and trichomonal vaginitis. After menopause, the commonest causes are senile vaginitis, senile endometritis and malignant lesions.
 - Marital state for the possibility of sexually transmitted diseases as Trichomonas vaginitis and gonococcal cervicitis.
 - Menstrual history: The date of last menstruation to exclude pregnancy.
 - Obstetric history: If the discharge starts after abortion or labour, it is usually due to cervical infection.

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- Present history: The duration, amount, character and odour of the discharge and its relation to menstruation. Symptoms of trichomonas infection often begin during or after menstruation (organism needs low acid medium).
- The presence of other symptoms as pruritus vulvae, dyspareunia, and urinary symptoms.
- General examination: For evidence of cachexia (malignant lesion).
- Abdominal examination: For a pelvi-abdominal swelling as fibroid or pregnancy.
- Pelvic examination:

The patient should not have a vaginal douche for at least 2 days before examination and has not used any vaginal medication for at least 5 days. The speculum and gloves must be sterile and dry. We must avoid any antiseptic or lubricant.

- Inspection of the vulva for vulvitis, Bartholinitis and the presence of discharge.
- A speculum is introduced.
 - The discharge collected in the posterior fornix is examined for the amount, character, and the presence of froth or blood.
 - The pH of discharge is estimated by a universal indicator.
 - A drop of discharge is taken, put on a slide and a drop of normal warm saline is added then examined microscopically for Trichomonas vaginalis, clue cells of bacterial vaginosis and Candida organism.
 - Another drop is taken for a Gram-stained film and a third drop is taken for culture.
 - Finally, the cervix and vagina are dried and inspected for any lesion.
- The urethra is milked and discharge obtained is examined by Gram-stained film and culture.
- Bimanual examination is performed to detect a lesion in the uterus or adnexa.

Special investigations:

These are done according to the clinical findings.

Urine for sugar and bilharzial ova; diabetes mellitus must be excluded in monilial vaginitis.

Stool analysis for oxyuris infection.

Serological test for syphilis if suspected.

Investigations to exclude malignancy; including cervical smear and biopsy from suspected lesions.

In infants, an X-ray or ultrasound may be done to exclude a foreign body.

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Sexually transmitted diseases

STD are infections acquired during sexual intercourse (heterosexual or homosexual), sometimes called venereal diseases. These diseases are caused by:

Bacteria: Gonorrhoea, chlamydial infections including lymphogranuloma venereum, soft sore, granuloma venereum.

Fungi: Tinea curis and vulvovaginal mycosis(candidiasis).

Spirochetes: Syphilis.

Viruses: Human papilloma virus, genital herpes, hepatitis B, hepatitis C, HIV, cytomegalovirus infection and molluscum contagiosum.

Parasites: Pediculosis pubis and genital scabies.

Gonorrhea

Etiology:

- Causative organisms. Neisseria Gonorrhea "Gonococci".
=> Gram negative diplococci, kidney shaped and mainly intracellular organism.
- Mode of transmission:
 - Sexual intercourse is responsible for the majority of cases.
 - Contamination from infected towels, instruments.etc.
 - Neonatal conjunctivitis (ophthalmia neonatorum) may be acquired during vaginal delivery.
- Site of infection:

The organism penetrates the columnar epithelium and to lesser extent transitional epithelium (but not stratified squamous epithelium).

Primary sites:

- a- The urethra and Skene's tubules.
- c- The Bartholin glands.

- b- The endocervix.
- d- The rectum.

Secondary sites: infection spread along the lumen of genital tract to affect:

- a- Endometrium (transient).
- c- Pelvic peritoneum.
- b- Tubes and ovaries.
- d- Bladder or pelvis of kidney.

Systemic infection with gonococci: as arthritis, iridocyclitis, hepatitis, meningitis and gonococcal septicaemia rarely occur.

Acute Gonorrhea:

Clinical picture:

Incubation Period: 2-8 days. It may be asymptomatic, and the clinical picture depends upon the site of infection.

- 1- Urethritis: frequency and burning micturition. Pus may be milked from the urethra.
- 2- Acute cervicitis.
- 3- Bartholinitis.
- 4- Vulvovaginitis: this occurs in children. There is a purulent vaginal discharge, vulval soreness and pruritis. The inguinal glands may be enlarged and tender.
- 5- Proctitis.

III. Infections of the female genital tract

6- Gonococcal tonsillitis or pharyngitis.

7- Pelvic infection: there are symptoms and signs of acute salpingitis or pelvic peritonitis in severe cases.

8- Gonococcal septicemia.

9- The Fitz-Hugh-Curtis syndrome:

- It occurs in about 5-10% of cases of acute salpingitis usually gonococcal or chlamydial.
- It is due to perihepatitis.
- The organisms reach the perihepatic area from the tubes by lymphatics or by spread along the peritoneal gutters with the circulating peritoneal fluid.
- Later on perihepatic adhesions is formed. These "Violin string" adhesions between the liver and diaphragm and anterior abdominal wall can be detected by ultrasound scan.

Investigations:

Specimens are taken from cervical canal, the urethra after milking, and by pressing on bartholin gland.

Gram-stained film.

Culture and sensitivity: Thayer-Martin medium.

The Gonozyne test: It is an enzyme immunoassay test which detects gonococcal antigen.

Treatment:

Prophylactic treatment: Prevention of sexually transmitted diseases.

1. Avoid promiscuous intercourse.
2. Avoid multiple partners.
3. Condom.
4. Screening and treatment of sexually transmitted disease.

Active treatment:

A. General treatment:

Avoid sexual intercourse till the patient is cured.

The husband and wife should be treated at the same time.

If there is acute salpingitis the patient should rest in bed at hospital.

B. Antibiotics:

- Ampicillin, erythromycin or tetracycline 500 mg / 6 hours for seven days.
- Doxycycline (vibramycin) 100 mg orally twice daily for 7 days.
- Ciprofloxacin 500 mg in a single oral dose. Azithromycin 1 g in a single oral dose.

NB: 30% of cases of gonorrhea can produce penicillinase enzyme. Erythromycin, tetracycline, doxycycline or azithromycin acts on both gonorrhea and Chlamydia. Ampicillin and erythromycin are safe in pregnancy.

C. Surgical treatment:

Any abscess as Bartholin abscess should be incised and drained.

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Chronic Gonorrhea:

Clinical picture:

- Chronic gonorrhoea is asymptomatic in 50% of cases.
- The clinical picture depends upon the site of infection so there may be evidence of chronic urethritis, chronic cervicitis or chronic salpingo-oophoritis.
- The Bartholin gland may be enlarged and tender, or it may be the site of recurrent abscess or cyst formation.

NB: Gonococci reaching the tubes die and disappear within 4 weeks after infection and are replaced by other organisms as streptococci and E.coli.

Investigations:

The diagnosis is proved by demonstrating the gonococci in smear and culture. Culture is essential for diagnosis.

Treatment:

An antibiotic to which the organism is sensitive is given and any residual lesion is treated according to its nature.e.g. cauterization for chronic cervicitis.

Chlamydial infection

Etiology:

Causative organisms: Chlamydia trachomatis

1. Gram negative intracellular bacterium.
2. There are several serotypes:
 - Serotypes A, B and C are associated with trachoma.
 - Serotypes D to K lead to genital infection in male and female.
 - Serotypes L1, L2 and L3 cause lymphogranuloma venereum.

Mode of transmission:

1. Sexual intercourse. It is the most common sexually transmitted disease in Sweden, the United States and many European countries.
2. Neonatal conjunctivitis results from transmission of organisms to the eyes during vaginal delivery (similar to gonococcus). 7-14 days.
 1. C. trachomatis is asymptomatic in about 75% of cases. Like gonococci the organism infects the columnar and transitional epithelium and ascends along the lumen of the genital tract. It leads to urethritis, bartholinitis, cervicitis, endometritis, salpingitis, peritonitis, proctitis and perihepatitis (Fitz-Hugh-Curtis syndrome).
2. Infertility.
3. During pregnancy the infection may cause abortion, preterm labor, premature rupture of membranes and postpartum endometritis.
4. The newborn may acquire inclusion conjunctivitis, otitis media and pneumonia during vaginal delivery.

Investigations:

The diagnosis is confirmed by one of the following tests:

1. Specimens: are obtained from urethral or cervical discharge.
2. Giemsa stain: It will show the intracellular bacterium.
3. Tissue culture: MacCoy medium. It is the most reliable method for diagnosis.

III. Infections of the female genital tract

4. Testing the maternal serum for antichlamydial antibodies. Unreliable because of the high false positive result.
5. Detection of chlamydial antigen in any clinical material by one of the following methods:
The immunofluorescent-stained smear.
The ELISA test (enzyme linked-immunosorbent assay) The DNA probe test. Reliable as culture.
The polymerase chain reaction (PCR) test. More rapid and more sensitive than culture.

Treatment:

Prophylactic treatment: Prevention of sexually transmitted diseases.

Active treatment:

A. General Treatment:

The husband and wife should be treated at the same time. Coitus is avoided during treatment.

Boiling of underwear.

B. Antibiotics:

Erythromycin or tetracycline 500 mg / 6 hours for seven days, 3 weeks in cases of lymphogranuloma venereum.

Doxycycline (vibramycin) 100 mg orally twice daily for 7 days. Azithromycin 1 g in a single oral dose.

NB: Erythromycin, tetracycline, doxycycline or azithromycin acts on both gonorrhoea and Chlamydia. Erythromycin is safe in pregnancy.

Syphilis

Etiology:

Causative organisms: *Treponema pallidum*

Motile spirochetes with special type of movement (Cork-screw movement).

Mode of transmission:

- 1- Sexually transmitted disease (STD).
- 2- Materno-fetal (Congenital syphilis).

Clinical picture:

Primary syphilis: (Incubation period: 10 - 90 days).

Chancre: Single, shallow punched out ulcer with well-defined edges (painless)

Usually present on the lower genital tract (cervix, vagina, clitoris, labium major, labium minor, fourchette) and urethra. The chancre may appear on other areas as the lips, mouth (oral sex) or anorectal region.

The chancre usually heals after 1-6 weeks.

The inguinal lymph nodes:

Painless, enlarged and do not suppurate.



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Secondary syphilis: (6 weeks to 6 months after the primary).

1. Generalized maculo-papular skin rash: on the trunk and limbs, bilateral and symmetrical (non-itchy and non-vesicular).
2. Mucous patches: Whitish areas seen on mucous membranes (e.g. inner aspects of lips, cheek, palate, cervix ... etc.) that ulcerate on removal.
3. Condylomata lata: Flat wart like growth on the vulva and perineum.
4. Generalized lymphadenopathy: especially epitrochlear lymph nodes.



Tertiary syphilis: (2-30 years)

1. Gumma: in any part of the body.
2. Cardiovascular lesions: e.g.: Aortic aneurysm.
3. Central nervous system: e.g.: Tabes dorsalis.

Investigations:

Specimens: are obtained from 1ry and 2ry lesions.

Microscopic examination:

- Dark field illumination to show the characteristic movement.
- Geimsa or Fontana stains.

Serological tests: (for detection of antibodies).

The serological test starts to be positive 2 weeks after appearance of the chancre.

Non-specific: (using non-treponemal antigens e.g. Cardiolipin lecithin antigen)

1. Wassermann reaction = complement fixation test.
2. VDRL (Venereal disease research laboratory test).
3. Rapid plasma reagin.

Specific:

1. Treponema pallidum immobilization test (TPI).
2. Fluorescent treponemal antibodies (FTA).

Treatment:

Prophylactic treatment: Prevention of sexually transmitted diseases.

Active treatment:

1- Primary and secondary syphilis:

Procaine penicillin 600.000 units I.M. daily for 10 days or the long- acting benzathine penicillin 2.4 million units I.M. (half the dose in each buttock).

For patients allergic to penicillin: oral erythromycin, tetracycline or cephalosporin 500 mg 6 hourly for 15 days.

2- All other syphilis (Latent, gummatous, neuron and cardiovascular):

Procaine penicillin 600.000 units I.M. daily for 20 days or benzathine penicillin 2.4 million units I.M. weekly for 3 weeks.

NB: Long-acting penicillin is contraindicated in neurosyphilis because it does not reach enough concentration in the cerebrospinal fluid.

For patients allergic to penicillin: oral erythromycin, tetracycline or cephalosporin 500 mg 6 hourly for 30 days.

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Condylomata acuminata

Etiology:

Causative organisms: Human Papilloma Virus (Papova virus).

1. It is ds DNA virus, non-enveloped.
2. More than 100 subtypes have been identified:
 - Low risk types; type 6, 11 → Condylomata acuminata.
 - High risk types; type 16, 18 → Cancer cervix.



Mode of transmission:

- Sexually transmitted disease (S.T.D.)
- Direct contact.
- Fetal infection: transplacental or across the birth canal => neonatal laryngeal papillomata.

Clinical picture:

- There are multiple small papillomata which usually grow in groups, rarely single.
- The warts appear on the vulva and around the anus and can affect the vagina, cervix, anal canal and lower part of the rectum.
- Heat and moisture stimulate the growth of warts.
- The condylomata grow more rapidly in women who are pregnant, diabetic, on combined oral contraceptives, and on immunosuppressant therapy.
- The human papilloma virus predisposes to carcinoma of the vulva, vagina, cervix and anorectal region.



Investigations:

- 1) Cytology using Papanicolaou smear shows characteristic cells known as koilocytes. The koilocyte is a large cell with a large hyperchromatic wrinkled nucleus, with a perinuclear halo.
- 2) Colposcopic examination of the cervix and vagina.
- 3) Biopsy taken from the lesion for histopathological examination.
- 4) D.N.A. hybridization technique:
 - Detect H.P.V.
 - Determine viral type

Treatment:

Small lesions less than 2 cm in diameter are painted with 25% podophyllin resin in liquid paraffin. The surrounding normal skin is covered with a protective as Vaseline.

1. It causes ischemia and necrosis of the warts.
2. It is contraindicated in pregnancy.
Trichloroacetic acid solution and 5-fluorouracil cream 5 % can be used.
Large lesions are treated by surgical removal, cryocautery, diathermy coagulation or laser vaporization.

Immunomodulator drugs can be used:

- Alpha-interferon: given systemically, inside the lesion or as topical cream.
- Imiquimod: a topical cream which elevates interferon levels.

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Genital herpes

Etiology:

- Causative organisms: "Herpes Simplex Virus"

1. Most cases are caused by HSV type 2, but it can be caused by type 1 (following oral sex).
2. It is DNA virus.
- Mode of transmission:
 1. Sexually transmitted disease (S.T.D.)
 2. Direct contact.
 3. Fetal infection: across the birth canal => disseminated neonatal infection.



Clinical picture:

- Incubation period: is 3-7 days.
- Fever, headache and malaise.
- The lesion affects the lower genital tract (cervix, vagina and vulva), perianal area and rectum.
- Vesicles appear which break down into multiple, small, shallow, very painful ulcers. There is erythema, discharge, edema.
- The inguinal nodes are often enlarged. Healing usually occurs by tenth day. Retention of urine sometimes due to local severe pain or sacral radiculitis.
- Recurrence of infection is common as the virus remains quiescent in the sacral ganglia.

Investigations:

Pap smear: Large multinucleated epithelial cells with intra-nuclear inclusion bodies.

Culture: Human amnion cell culture.

D.N.A. probe technique or PCR.

Treatment:

Acyclovir oral tablets, one tablet (200 mg) 5 times daily for 5 days.

Acyclovir is given intravenously in severe cases.

In mild, recurrent disease acyclovir cream may be enough. It is applied 5 times daily for 5 days.

Famciclovir: can be used.

Lymphogranuloma Venereum

Etiology:

Caused by: Chlamydia trachomatis (serotypes L1, L2, L3).

Incubation period: 7-14 days.

The lesion:

- Start as papule or vesicle on the vulva or perianal area then forms an ulcer.
- The disease spreads by lymphatics causing inguinal adenitis. The nodes are matted together and tend to breakdown to form multiple abscesses. Chronic lymphatic obstruction can result in vulval elephantiasis. Rectal stricture and fistulas are frequent.

Treatment: As Chlamydia (3 weeks).

Suppurating inguinal lymph nodes (Bubos) are aspirated as incision is contraindicated.

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Granuloma Inguinale

Synonyms: Granuloma venerium - Donovanosis

Etiology:

Caused by: **Donovan bodies** (intracellular G -ve bacilli). (*Calymmatobacterium granulomatis*)

Incubation period: 10-40 days.

The lesion:

- Ulcer in labia or vagina (centre of the ulcer heals but the border active).
- L.Ns: enlarged inguinal LNs but don't suppurate and this differentiates the lesion from LGV.

Investigations:

Smear: Giemsa stain show Donovan bodies which appear as cluster within the cytoplasm of cells.

Culture: yolk sac of chick embryo.

Treatment:

Erythromycin or Tetracycline 500 mg / 6 hours for 21 days.

Chancroid (Soft sore)

Etiology:

Caused by: **Haemophilus Ducreyi** (gram -v bacilli).

Incubation period: 2-5 days.

The lesion:

- Start as papule then form pustule that rupture leaving soft sore. Ulcers: multiple, small and very painful.
- L.Ns: enlarged, suppurative and tender.

Investigations:

Smear: **gram stain show gram -ve bacilli.**

Culture: **enriched media.**

Treatment:

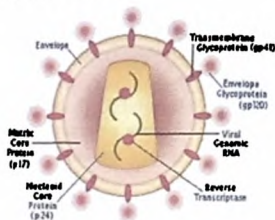
Erythromycin or Tetracycline 500 mg / 6 hours for 21 days

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Acquired Immunodeficiency Syndrome

Causative organisms:

- Acquired Immunodeficiency Syndrome (A.I.D.S.) is caused by one of the retroviruses, HIV (human immuno-deficiency virus) type I and II.
- It has: Double stranded R.N.A. with reverse transcriptase.
- Envelope associated with 3 glycoproteins that identify the CD4 cells (T-helper cells).
- Once the virus becomes inside the cell (T-helper), R.N.A is converted into D.N.A. (by reverse transcriptase enzyme) that is incorporated with D.N.A. of the affected cell for long latent period then activation occurs due to unknown mechanism leading to death of T-helper cells and so, decrease their number.



Mode of transmission:

Sexually transmitted.

Parental transmission: blood transfusion, blood products, infected syringes, instruments.

Maternofetal (vertical) transmission.

Clinical picture:

Incubation period: Variable from 2-10 years.

Clinical picture

- Opportunistic infections: pneumonia
 - Kaposi sarcoma ... etc. AIDS related complex.
 - Weight loss >10 % in < one month.
 - Fever > one month.
- Recurrent infections e.g. monilial infection etc.
- Diarrhea > one month.
- Generalized lymphadenopathy.

Investigations:

Serological tests: Detection of antibodies.

Screening: ELISA.

Confirmation:

- Western blot technique.

P.C.R.

(polymerase chain reaction).

Laboratory tests:

1. Complete blood picture.
2. Decreased Th / Ts ratio.

Treatment:

Prophylactic treatment

- Prevention of sexually transmitted diseases.
- Prevention of parental transmission.

Active treatment:

- Zidovudine, lamivudine and saquinavir.

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Genital Tuberculosis

Etiology:

- Causative organisms:

Mycobacterium tuberculosis.

Human type: 95 % (1 ry complex in the lungs).

Bovine type: 5 % (1 ry complex in the intestine).

- Mode of transmission

Genital T. B. is always 2ry to a primary focus. It is either: Spread by blood or lymph from a primary lesion elsewhere in the body as the lungs or bronchial lymph nodes (blood stream) or mesenteric lymph nodes (by lymphatics).

Direct spread from tuberculous peritonitis or tuberculous mesenteric glands.

Ascending infection with tuberculous semen or sputum.

- Predisposing factors: Poverty, malnutrition and Diabetes mellitus.

Prevalence: It varies greatly according to the socio-economic conditions. In USA, < 1% of infertile women have genital tuberculosis and in India the figure is 13%.

Pathology:

Tuberculosis of the tube: (> 90% of cases)

The infection is bilateral in the majority of cases. Infection may be:

- Tuberculous perisalpingitis: Military tubercles appear on the peritoneal coat of the tube. It is a part of tuberculous pelvic peritonitis.
- Tuberculous interstitial salpingitis: The wall of the tube is thick and fibrous. The muscle layer shows caseous foci. The tube is tortuous and surrounded by adhesions.
- Tuberculous endosalpingitis: Infection starts in the mucosa which becomes infiltrated and necrotic. The tube may become distended by thick caseous material forming a tuberculous pyo-salpinx which is sausage-shaped and not retort-shaped because distension usually starts at the isthmic end.

Tuberculosis of the uterine body: (45%)

- Infection is always secondary to a tubal lesion. In early cases tubercles appear in the endometrium near one or both cornua or in the region of the internal os. Gradually, the endometrium becomes replaced by tuberculous granulation tissue.
- Tuberculous pyometra may result.
- In advanced cases, the myometrium becomes involved.

Tuberculosis of the ovaries: (30%)

- Mostly occurs as a direct extension from the tube. The ovary may look normal on naked eye appearance; however, the disease may be manifested by surface tubercles, extensive adhesions or tuberculous abscesses.

Tuberculosis of the cervix: (10%)

- The lesion takes the form of polypi or ulcers.
- Tuberculous ulcers are single or multiple. The ulcer has a serpiginous outline, undermined edge and a yellow floor. The base is soft.

Tuberculosis of the vagina and vulva: (1%)

The lesion takes the form of polypi or ulcers.

III. Infections of the female genital tract

Microscopic picture (Tubercle)

Showing the following layers: central caseation, lymphocytes, giant cells and Epithelioid cells.

Diagnosis:

The possibility of tuberculosis is suspected in the following cases: family history of tuberculosis, history of exposure to infection, patient coming from an endemic area, idiopathic infertility, and chronic pelvic infection in a virgin or which is resistant to treatment.

Symptoms:

- 1) Asymptomatic: The condition may be asymptomatic.
- 2) General symptoms of tuberculosis may be present in the form of loss of appetite, loss of weight, excessive sweating and night fever.
- 3) Infertility: the commonest complaint. It is due to anovulation resulting from ovarian tuberculosis and bad general condition, blocked tubes, and destruction of the endometrium preventing implantation of the ovum.
- 4) Pain in the form of dull ache in the lower abdomen.
- 5) Symptoms of pelvic congestion in the form of congestive dysmenorrhoea, menorrhagia and increased normal vaginal discharge (leucorrhoea).
- 6) Menstrual disturbances: oligomenorrhoea and amenorrhoea. Menorrhagia, metrorrhagia and postmenopausal bleeding may occur.

General examination: This may reveal a tuberculous lesion elsewhere in the body as the lungs.

Abdominal examination: It may show tuberculous peritonitis.

Vaginal examination:

Inspection for tuberculous lesions in the vulva.

Bimanual examination: the uterus feels normal or slightly enlarged, the tubes are normal, thickened or an adnexal swelling is felt which is fixed, tender and indurated.

Small nodules may be felt in Douglas pouch.

Speculum examination reveals lesions in the cervix or vagina.

Investigations:

General:

- Blood picture (anemia, leukopenia with lymphocytosis and increased E.S.R.).
- Sputum examination: for acid fast bacilli (Z.N. stain).
- Chest X-ray.
- Tuberculin test: good negative but not reliable if positive in endemic areas.

Specific:

Genital tract biopsy:

- Direct biopsy from any ulcer or mass in cervix, vagina and vulva.
- Laparoscopic biopsy from tubal lesions.
 - Premenstrual endometrial biopsy. This is examined by stained film (Ziehl-Neelsen stain) and culture on specific media as Lowenstein-Jensen medium.

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Hysterosalpingogram (HSG):

- It is contraindicated in cases with active T.B. infection.
- If done for cases of infertility, it may reveal one of the following pictures:
 - * Kinking of the tube.
 - * Beaded tube (salpingitis isthmica nodosa).
 - * Pipe stem.
 - * Pyosalpinx.
 - * Bilateral tubal block.
 - * Lymphatic intravasation.

Endoscopy:

Laparoscopy: Laparoscopic findings in case of T.B. salpingitis: 1- Sausage shape with tubercles on the surface.

2- Fimbriae are projecting like a tuft (not indrawn) with caseous material coming out.

3- The tube looks pale with calcific spots (calcified tubercles) on its wall.

Hysteroscopy: for T.B. endometritis.

Colposcopy: for cervical and vaginal lesions.

P.C.R. (polymerase chain reaction): recently used to detect T.B.

Treatment:

Medical:

- Admission to hospital may be indicated when an active extragenital lesion is present.
- Nourishing diet, tonics and vitamins.
- Chemotherapy: the following treatment is given for 9 months.
- Three drugs are given for 2 months: isoniazid + rifampicin + ethambutol or streptomycin. This is followed by isoniazid and rifampicin given for 7 months.
- I. N.H. (Isoniazid): 300mg / day.
- Rifampicin: 450-600mg /day.
- Streptomycin: 1 gm / day IM.
- Ethambutol: 15 mg/kg body weight/day.

Surgical:

- Indicated if medical treatment fails and in the presence of large masses.
- For tuberculous adnexa: total hysterectomy and bilateral salpingo-oophorectomy.
- Surgery is preceded and followed by medical treatment for at least 3 months.
- Drains should not be used to avoid fistula formation.

Prognosis:

The pregnancy rate after medical treatment is 20%. However, one third will abort, one third ectopic pregnancy occurs and one third will continue to full term.

Genital Bilharziasis

Etiology:

- Causative organisms are *Schistosoma haematobium* or *mansoni*.
- The ova are deposited in the submucous or subcutaneous tissues with formation of bilharzial granulation tissue.
- In late cases fibrosis occurs. Calcification may occur in longstanding lesions.
- The commonest sites affected are vulva, vagina and portio-vaginalis of the cervix.

III. Infections of the female genital tract

Clinical picture:

Bilharziasis of the vulva:

- Any area of the vulva or the perineum can be affected. The lesion takes the form of papillomata or ulcers.
- The papillomata are small, sessile, firm and usually multiple. They are dark red in colour with occasional areas of calcification. The presence of multiple papillomata leads to pseudo-elephantiasis.
- The ulcers are superficial and multiple.

Bilharziasis of the vagina:

- This appears in the form of multiple papillomata, ulcers, sandy patches or vaginal stenosis due to fibrosis.
- The symptoms are vaginal discharge, irregular vaginal bleeding and dyspareunia.

Bilharziasis of the cervix:

- The portio-vaginalis of the cervix is the commonest site of genital bilharziasis.
- The lesion takes the form of ulcers or papillomata which may be single or multiple. The main symptoms are vaginal discharge, irregular vaginal bleeding and infertility.
- Bilharzial antibodies are spermatotoxic.

Bilharziasis of the uterine body:

It may affect the endometrium or myometrium. Irregular uterine bleeding is the main symptom. The lesion is very rare due to monthly shedding of the endometrium.

Bilharziasis of the tubes and ovaries:

- Usually bilateral. Lesion in the tube may be localized (salpingitis isthmica nodosa) or diffuse and predisposes to ectopic pregnancy.
- The ovary is usually enlarged with thickened tunica albuginea and may show hard nodules on the surface.
- The main symptoms are lower abdominal pain, congestive dysmenorrhoea and infertility (blocked tubes).

Diagnosis:

- Young age of the patient.
- Residence in an endemic area. History of terminal haematuria.
- Symptoms and signs suggestive of bilharziasis. Urine and stool analysis.
- Cystoscopy and proctoscopy.
- Demonstration of bilharzial ova by biopsy, vaginal smear or scraping from ulcers. Bilharzial ova can be seen through the colposcope.
- Complement fixation and precipitation tests.

Complications:

1- Urinary fistula. 2- Infertility.

Treatment:

Medical treatment:

- Anti-bilharzial drugs as Praziquantel (40mg/kg body weight). Antibiotics if there is secondary infection.
- Treatment of associated anemia.

Surgical treatment:

Removal of any masses.

III. Infections of the female genital tract

Miscellaneous infections

Endometritis

Etiology:

- Senile endometritis.
- Tuberculous endometritis.
- Puerperal endometritis and septic abortion. Gonoccal endometritis.
- Non specific endometritis (after curettage, IUCD insertion and on top of degenerated submucous fibroid).

Senile endometritis

Symptoms:

General symptoms of infection as fever and rigors. Suprapubic pain.
Intermittent purulent vaginal discharge.

Signs:

- Patient is feverish and toxic.
- The uterus is symmetrically enlarged, soft, and tender.
- The passage of a uterine sound is followed by a discharge of pus.

Investigations:

Pus is sent for aerobic and anaerobic culture and sensitivity test.

Treatment:

1. *Drainage of pus.*
2. *Ecbolics to help drainage by contracting the uterus.*
3. *Antibiotics according to culture and sensitivity test.*
4. *Uterine curettage is done one week after drainage to exclude a malignant tumour*
5. *Hysterectomy for resistant cases.*

Pyometra

It is a collection of pus within the uterus.

Etiology:

- Endocervical carcinoma. Endometrial carcinoma. Senile endometritis.
- Puerperal endometritis and septic abortion.
- Congenital atresia of cervix or vagina.
- Stenosis of cervix or vagina following operations or radiotherapy. Infected submucous fibroid.
- Intrauterine contraceptive device.

Clinical picture:

(A) Symptoms:

- General symptoms of infection as fever and rigors. Suprapubic pain.
- Intermittent purulent vaginal discharge.

(B) Signs:

- Patient is feverish and toxic.
- The uterus is symmetrically enlarged, soft, and tender.
- The passage of a uterine sound is followed by a discharge of pus.

III. Infections of the female genital tract

Investigations:

Pus is sent for aerobic and anaerobic culture and sensitivity test.

Treatment:

1. Drainage: Under general anaesthesia, the cervix is dilated and a rubber tube is fixed for drainage.
2. *Ecbolics* to help drainage by contracting the uterus.
3. Antibiotics, according to culture and sensitivity test.
4. Uterine curettage is done one week after drainage to exclude a malignant tumour.
5. Hysterectomy for resistant cases.

Toxic shock syndrome

Etiology:

- The syndrome is caused by the *Staphylococcus aureus* which multiplies in the vagina of women who are using tampons for menstrual protection.
- The organism introduced into the vagina on the inserting fingers, will multiply in the retained menstrual blood and produces an exotoxin which is absorbed through the vaginal wall into the circulation.
- About 10% of pregnant women harbor *Staphylococcus aureus* in the vagina, and so, the syndrome can occur in postpartum period.

Clinical features:

- Symptoms start between the second and fourth day of menstruation.
- Fever, headaches, nausea, vomiting, watery diarrhea, hypotension, muscle ache, skin erythema and subcutaneous edema.
- There is affection of the liver, kidneys, myocardium, thrombocytopenia and sometimes disseminated intravascular coagulation.
- Confusion and death may occur (3-6%).

Prevention:

- General hygiene with care in handling and inserting menstrual tampons.
- Reduce collection of blood in the vagina by changing the tampons 3-4 times by day and using an external pad at night.

Management:

Remove the tampon, take cultures from it and from the upper vagina as well as blood culture.

Antistaphylococcal antibiotic is given.

Resuscitation and treatment of shock, this is best carried out in an intensive care unit because there is multisystem failure.

After recovery, further cultures are taken from the vagina to exclude a carrier state as the syndrome is liable to recur (30%).

IV. Uterine Fibroids

Uterine fibroids

Definition and synonyms:

- Leiomyoma is a benign neoplasm arising from smooth muscle fibers.
- However, the tumor contains connective tissue fibers as well and so, it is also called myofibroma or fibromyoma.
- Fibroid is the commonest term.

Incidence:

- About 20% of women above the age of 35 have fibroids. Fibroid is the commonest pelvic tumor.
- Age: between 35-45 years.
- Race: More common in black women.
- Parity: More common in nulliparae and women with low parity.
- Family history: There is a familial tendency to develop fibroids. Certain genes on chromosomes 7 and 12 are related to the pathogenesis of fibroids.

Etiology:

- The exact etiology is unknown.
- The tumor is estrogen dependent and excessive estrogen stimulation predisposes to fibroids

Site of origin:

- *Corporeal fibroid (97% of cases)* arises in the body of uterus. Fibroids in the uterine body may be interstitial (intramural), subserous or submucous.
- *Cervical fibroid (3% of cases)* arises in the cervix.
- *Special types* include submucous fibroid polyp, pedunculated subserous fibroid, broad ligamentary fibroid and intravenous leiomatosis.

Pathology:

- Size: It varies from very small fibroids (seedlings) to huge tumors filling the whole abdomen.
- Shape: The fibroid starts as a small spherical tumor but as it enlarges its shape may be changed by compression.

Consistency:

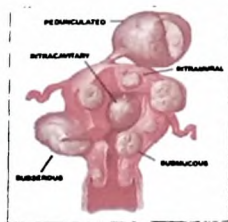
- Firm unless affected by degeneration.
- The tumor becomes soft during pregnancy or due to hyaline or cystic degeneration.
- It is hard when calcified.

Macroscopic appearance:

- The tumor is white in color because it is poor in blood supply.
- The cut surface shows a whorled appearance due to interlacing of muscle and connective tissue fibers.
- The interstitial fibroid is surrounded by a false capsule made of compressed uterine muscle. The capsule contains blood vessels which supply the tumor and it is the source of bleeding during myomectomy.

Microscopic appearance:

- The tumor is composed of smooth muscle fibers in a connective tissue.
- The nucleus of the muscle cell is thick, short with rounded ends.
- The nucleus of the fibroblast is thin and filiform.



IV. Uterine Fibroids

- By the Van Gieson stain, the muscle fibers appear yellow and the connective tissue fibers appear red.

Blood supply of fibroids:

1. Interstitial fibroid receives blood vessels from the surrounding capsule. the vessels pass radially towards the center of the tumor and so if calcification occurs, it starts at the periphery of the tumor as calcium is deposited from blood, also hyaline degeneration always starts at the center of the tumor which is poor in blood supply.
2. Subserus fibroid receives blood vessels from the pedicle because the peritoneal coat is not vascular.
3. Submucous fibroid receives blood vessels from the pedicle and from the covering endometrium.

Secondary pathological degenerative changes and complications of fibroids:

- Atrophy.
 - Necrosis.
 - Degeneration.
 - Vascular changes.
 - Malignancy.
 - Infection.
 - Torsion.
 - Incarceration.
 - Inversion of the uterus.
- Atrophy:
 - Tumor shrinkage normally occurs after menopause and in the puerperium due to lack of estrogen and reduced blood supply to the uterus.
 - Necrosis:
 - Due to complete cutting of the blood supply of the tumor leading to death of tissue.
 - Necrosis may occur after torsion of a subserus fibroid or application of intracavitary radium.
 - Degeneration:
 - a. Hyaline degeneration:
 - It is the commonest degeneration.
 - It usually starts at the center of a large tumor because it is the least vascular area.
 - The affected area is replaced by hyaline material and appears structure less, homogeneous and loses its whorled appearance.
 - Clinically, the patient may complain of dull aching pain and the tumor becomes soft in consistency.
 - Sometimes, the hyaline material liquefies forming cystic spaces filled with colorless or blood-stained fluid.
 - b. Cystic degeneration:
 - It is the result of liquefaction of hyaline material leading to the formation of cystic spaces.
 - The condition may also follow red degeneration, dilatation of blood vessels (telangiectasis) or lymphatics (lymphangiectasis).
 - Clinically, the tumor becomes soft or cystic in consistency and may be mistaken for a pregnant uterus.
 - c. Fatty degeneration:
 - Fat globules are deposited inside the muscle fibers or in between the fibers (fatty infiltration).
 - The tumor becomes soft in consistency and yellow in color.
 - d. Calcification:
 - It is usually preceded by fatty degeneration.
 - It occurs in tumors with poor blood supply and so it usually occurs after menopause and in subserus fibroids.
 - Calcium salts (carbonate or phosphate) are deposited from the blood and so calcification is found at the periphery of the tumor and along the blood vessels passing radially towards its center. Sometimes, the whole tumor becomes calcified (womb stone).

IV. Uterine Fibroids

- Clinically, the tumor becomes stony hard in consistency and gives a characteristic X-ray shadow (honeycomb like calcification).
 - e. **Red degeneration (necrobiosis):**
 - It is incomplete necrosis from which the tissues can recover.
 - It affects interstitial fibroids.
 - It may occur during pregnancy (usually in the second trimester), labor, puerperium and very rarely with combined contraceptive tablets and in postmenopausal women receiving estrogen replacement therapy.
 - The tumor becomes soft, red in color (salmon pink) and may give a fishy odor due to secondary infection with *E. coli*. The staining is due to diffusion of hemoglobin pigment throughout the tumor.
 - Microscopically, there is thrombosis in the blood vessels of the capsule.
 - The true cause is unknown, but it is believed that thrombosis occurs in the blood vessels of the capsule leading to ischemia and incomplete necrosis of the tumor. The ischemic cells produce a lipoid toxin which causes intravascular hemolysis, then hemoglobin diffuses out of the blood vessels staining the tumor red.
 - The patient complains of sudden onset of severe abdominal pain localized over the affected tumor and may be accompanied with vomiting. Mild fever usually occurs after some hours due to absorption of hemoglobin.
 - On palpation, the tumor is very tender.
 - Treatment is mainly medical by rest in bed, and analgesics for pain.
 - **Vascular changes:**
 - Edema and this is common during pregnancy and also occurs when the tumor becomes impacted in the pelvis.
 - Congestion due to torsion of a subserous fibroid.
 - Telangiectasis.
 - Lymphangiectasis usually due to severe edema.
 - **Malignancy:**
 - Change into sarcoma is rare and occurs in one to 5 per thousand cases.
 - It is a leiomyosarcoma or fibro sarcoma.
 - The affected area loses the whorled appearance; it becomes soft and yellow in color with areas of hemorrhage and necrosis.
 - Malignancy is suspected in the following conditions:
 - Rapid growth of the tumor.
 - Growth of the tumor after menopause.
 - Features suggesting malignancy as loss of weight and cachexia.
 - **Infection:**
 - This may occur in the following conditions:
 - Fibroid polyp usually becomes ulcerated and infected at its lower pole due to poor blood supply.
 - Submucous fibroid may become infected after abortion, labor, curettage.
 - Subserous fibroid may become infected from a neighboring organ as bowel or appendix.
 - Infection may follow red degeneration.
 - Infection from the bloodstream which is rare.
-

IV. Uterine Fibroids

- Clinically, the patient may complain of dull aching pain and fever. The tumor becomes soft and tender.
- Torsion:
 - Torsion of a pedunculated subserous fibroid leads to acute abdominal pain.
 - Rupture of a vein on the surface of a subserous fibroid leads to internal hemorrhage.
- Inversion of the uterus:
 - Inversion of uterus caused by a fundal submucous fibroid or fibroid polyp.

Clinical picture:

I. Symptoms:

A- Asymptomatic: In about 50% of cases, the condition is symptomless and is discovered accidentally.

B- Symptomatic: The patient may complain of one or more of the following:

I- Abnormal uterine bleeding:

1- Menorrhagia: The commonest symptom and is caused by:

- Increased vascularity of the uterus.
- Endometrial hyperplasia.
- Increase in the surface area of the endometrium due to enlargement of the uterine cavity.
- The presence of fibroids mechanically interferes with uterine contractions which help to stop the bleeding.
- Associated anovulation.

2- Polymenorrhea: It is due to ovarian congestion which is a part of pelvic congestion caused by the presence of fibroids. Ovarian congestion causes early degeneration of the corpus luteum.

3- Metrorrhagia: It is due to:

- Ulceration of a submucous fibroid or a fibroid polyp.
- Malignant change in the fibroid.
- Associated lesions as endometrial polypi, endometrial carcinoma and dysfunctional uterine bleeding.

II- Vaginal discharge:

- Watery discharge due to pelvic congestion and increased surface area of the endometrium.
- Purulent or blood-stained discharge due to ulceration and infection of a fibroid polyp.

III- Pain: This may be in the form of:

- Congestive dysmenorrhea.
- Colicky pain caused by uterine contractions to expel a fibroid polyp.
- Lower abdominal pain and heaviness caused by large tumors.
- Pain due to complication for example red degeneration or torsion of a subserous fibroid causes acute abdominal pain; hyaline degeneration causes dull aching pain, infection causes pain and fever, also pain may be caused by malignant change.
- Pain due to associated lesions as salinities or endometriosis.

IV- Infertility:

- Present in about 30% of cases and may be caused by:
- Mechanical obstruction by a cervical fibroid (cervical factor).

IV. Uterine Fibroids

- A submucous fibroid may prevent implantation of the ovum or causes early abortion (uterine factor).
- Blocked tubes by corneal fibroids, broad ligament tumor or associated salpingitis (tubal factor).
- Anovulation due to thickened tunica albuginea (ovarian factor).
- Increased distance for sperm to travel.
- About 40% of women will conceive after myomectomy. However, all other causes of infertility should be excluded before deciding that the myoma is the cause.

V- Abdominal mass: This may be the only complaint particularly with a large subserous fibroid.

VI- Pressure symptoms:

- These are more liable to occur with a cervical fibroid which may cause renal colic, frequency of micturition, dysuria, acute retention or chronic retention with overflow.
- Pressure on the rectum leads to constipation and piles.
- Also, a large abdominal tumor may cause dyspnea and palpitation.

VII- General symptoms:

- Symptoms of anemia as headache and palpitation if there is excessive blood loss.
- Symptoms of polycythemia which is a rare finding. It is usually caused by a large myoma in the broad ligament. The explanation is unknown but the tumor may compress the ureter and affect the erythropoietic function of the kidney or the tumor itself produces erythropoietin.

VIII- Symptoms of complications.

II. Signs:

1- General examination:

Signs of anemia if there is excessive bleeding.

2- Abdominal and pelvic examination:

- If the tumor is more than the size of 12-week pregnancy, it will give rise to a pelvi-abdominal mass. If less than the size of 12-week pregnancy, it will give rise to a pelvic mass.
- Typically, the uterus is irregular or knobby due to the presence of multiple fibroids.
- It is firm in consistency, mobile and not tender.
- Vaginally, the swelling is continuous with the uterus and moves with movement of the cervix.
- If a uterine sound is introduced, it will show enlargement of the uterine cavity in case of submucous and interstitial fibroids.
- Bimanual examination shows that the uterus is enlarged and firm. The enlargement may be symmetrical or asymmetrical in the presence of multiple fibroids.
- A pedunculated subserous fibroid may be mistaken for an ovarian tumor.
- A broad ligament fibroid is felt on one side of the uterus and displacing it laterally to the other side.
- A cervical fibroid is felt as a fixed firm swelling with the uterus on its top.
- With speculum examination, a fibroid polyp may be seen coming from the cervical canal.

Investigations:

1. Pelvic ultrasonography (either transabdominal or transvaginal): This shows the size, site and number of fibroids and differentiates the tumor from other swellings as ovarian tumor.
2. Saline infusion sonography (sonohysterography), where saline is injected into the uterus during ultrasound allows better detection of a submucous myoma.

IV. Uterine Fibroids

3. Hysterosalpingography (HSG): If infertility is a complaint, HSG confirms tubal patency and may reveal a submucous fibroid or a small fibroid polyp which appears as a filling defect.
4. Hysteroscopy may be used to diagnose a submucous fibroid or a small fibroid polyp.
5. Endometrial biopsy is done if there is irregular uterine bleeding to exclude associated endometrial carcinoma.
6. Intravenous pyelogram is done in cases of cervical and broad ligament fibroid to show the course of ureter, to diagnose hydroureter and hydronephrosis and to assess kidney function.
7. CT scan or MRI may be helpful in difficult cases when ultrasound cannot differentiate between myoma and localized adenomyosis and between broad ligament fibroid and ovarian tumor.
8. Other investigations to prepare the patient for operation.

Differential diagnosis:

- Causes of a pelvi-abdominal swelling as ovarian tumor.
- Causes of symmetrically enlarged uterus as diffuse adenomyosis.
- Fibroid polyp is to be differentiated from any mass protruding from the cervix as chronic inversion of uterus.
- A broad ligament fibroid may be confused with a broad ligament cyst or a tubal mass as hydro- or pyo-salpinx.
- Posterior wall fibroid has to be differentiated from other masses felt in Douglas pouch.

Treatment:

1) Expectant management:

Small symptomless fibroids require no treatment but the patient is kept under observation and examined clinically and by ultrasound every 6 months.

2) Medical treatment:

Hormonal:

- Menorrhagia is temporarily controlled by a progestogen, COCPs.
- Gonadotrophin releasing hormone analogue (agonist) is the most recent medical treatment. It is given for three months. It leads to amenorrhea and reduction of tumor size by 25-50%. This makes subsequent operation easier and with less blood loss. However, it leads to osteoporosis if used more than 6 months and rapid re-growth of the myoma occurs after cessation of treatment.
- Mifepristone can be given in a dose of 50 mg/day for 3-6 months. It reduces the size of myomas by 50%.
- Mirena coil treats menorrhagia, and reduces the size of fibroids.

Non-hormonal:

Antiprostaglandins, tranexamic acid.

3) Surgical treatment:

Indications:

- **Large tumors:** If the size of the tumor is more than 12-week pregnancy. This is a matter of controversy.
- **Symptomatic tumors** not responding to medical treatment as surgical treatment is the main line unless there is absolute contraindication to surgery.

IV. Uterine Fibroids

a) Myomectomy:

Definition:

It means removal of fibroids from the uterus leaving behind the organ to carry its function which is menstruation and pregnancy.

Indications:

- It is the operation of choice in all women below the age of 40 who want to become pregnant.
- A small fibroid polyp not larger than 8-week pregnancy is removed by vaginal myomectomy.
- A submucous fibroid less than 5 cm in diameter is removed using the hysteroscope.

Contraindications:

- If the patient is above the age of 40.
- Multiple fibroids when it is found that the operation will leave behind a useless organ.
- Cervical fibroid is usually treated by hysterectomy.
- If malignancy is suspected.

The presence of other lesions in the uterus as adenomyosis.

Types:

Abdominal myomectomy.

Vaginal myomectomy.

Hysteroscopic myomectomy (for submucous fibroid less than 5 cm in diameter).

Laparoscopic myomectomy (for pedunculated subserous fibroid).

b) Hysterectomy:

- Indicated when myomectomy is contraindicated. It may also be indicated in case of uncontrollable bleeding during myomectomy.
- Hysterectomy may be subtotal or total.
- If the patient is 50 years or above, we remove both ovaries.

4) Embolization of both uterine arteries:

- For angiographic embolization, a local anesthesia is given and a catheter is passed along the femoral artery to reach the aorta. A radio-opaque dye is injected to show the pelvic arteries. A catheter is then passed to block the uterine artery on both sides using small pieces (2 x 2 x 2 mm) of Gelfoam or other material.
- The tumor size is reduced by about 50%.
- It may be complicated by uterine infection in the form of endometritis and pyometra as well as infection of the necrotic fibroids.
- Indicated when patient is unfit for hysterectomy or refuses it.

5) MRI-guided Focused Ultrasound (MRI-FUS):

- This technique is a noninvasive thermal ablation device integrated with MR imaging system for the ablation of soft tissue.
- It has a potential role as a fertility conserving option.



IV. Uterine Fibroids

Cervical fibroid

Incidence:

- The neoplasm arises from the smooth muscle fibers of the cervix.
- It accounts for about 3% of all fibroids and is usually single.

Types:

- Fibroid arising in the supravaginal portion of the cervix: It remains interstitial and causes displacement and compression of one or both ureters.
- Fibroid arising in the portio vaginalis of the cervix: It remains interstitial causing barrel-shaped enlargement of the cervix or it forms a cervical polyp.

Symptoms:

Pressure symptoms:

- These may take the form of renal colic, frequency of micturition, dysuria or acute retention of urine as the cervical fibroid stretches the urethra and interferes with the opening of the internal urethral sphincter.
- Retention usually occurs few days before menstruation due to premenstrual pelvic congestion which causes enlargement of the fibroid.
- Pressure on the rectum leads to constipation and piles
- Infertility: Due to obstruction of the cervical canal.

Vaginal discharge: Due to ulceration and infection of a fibroid polyp.

Dyspareunia: Caused by a large cervical polyp.

Metrorrhagia: If ulcerated.

Signs:

- A large interstitial cervical fibroid is felt as a firm fixed pelvic mass with the uterus lying on its top.
- The tumor arising in the portio vaginalis causes barrel-shaped enlargement of the cervix or forms a cervical polyp.

Treatment:

- The interstitial cervical fibroid is usually treated by abdominal hysterectomy as myomectomy is difficult (difficult to control bleeding and to obliterate the dead space left after myomectomy). Before operation, an intravenous pyelogram is done to show the course of the ureters and assess kidney function.
- A cervical fibroid polyp is removed by vaginal polypectomy (myomectomy).



IV. Uterine Fibroids

Uterine polypi

Corporeal polypi

1- Adenomatous or mucus polyp:

- It arises from the endometrium.
- Types:
 - a) **Multiple polypi**: these result from stimulation of the endometrium by excessive oestrogen as in case of PCO, fibroids, or endometriosis. This is the commonest uterine body polyp.
 - b) **Single adenomatous polyp**: which is an adenoma of the endometrium. It is composed of endometrial glands in a connective tissue stroma and covered by columnar epithelium.
- Adenomatous polypi cause menorrhagia and sometimes intermenstrual bleeding.
- Diagnosis is easy if the polyp protrudes from the cervix, otherwise, diagnosis cannot be made except by uterine curettage, hystero-graphy or hysteroscopy.
- Treatment is by uterine curettage. A single polyp is removed by sponge forceps or hysteroscope. Histopathological examination is necessary to exclude malignancy.

2- Fibroid polyp:

The polyp forms a firm mass, its tip is liable to necrosis and infection due to poor blood supply. A rare complication is chronic inversion of uterus.

Symptoms :

- 1- Menorrhagia.
- 2- Irregular vaginal bleeding due to necrosis and ulceration of the tip of the tumor.
- 3- Offensive vaginal discharge due to infection of the polyp.
- 4- Colicky pain due to uterine contractions trying to expel the tumor.

Treatment : vaginal myomectomy or hysterectomy.

3- Placental polyp:

If a placental fragment is retained in the uterus after an abortion or labor, blood becomes coagulated in layers over the retained fragment forming a polyp which is dark red in color and firmly adherent to the wall of the uterus. The uterus is subinvolved and the cervix may remain dilated.

Treatment is curettage and histological examination to exclude choriocarcinoma.

4- Malignant polyp:

Malignant change may occur in a fibroid or adenomatous polyp. Primary malignant tumor as carcinoma, sarcoma or choriocarcinoma may form a polyp projecting into the uterine cavity.

IV. Uterine Fibroids

Cervical polyp

1-Adenomatous or mucus polyp:

Pathology:

It arises from the endocervix. In the majority of cases it is the result of chronic cervicitis. The polyp is composed of cervical glands embedded in a connective tissue stroma and covered by columnar epithelium. The polyp appears as single or multiple, soft swelling projecting from the external os.

Treatment:

Surgical excision with cauterization of the base of the polyp to prevent recurrence. Curettage of the cervical canal is performed to prevent recurrence because there is usually hyperplasia of the endocervical mucosa.

2- Fibro-adenomatous polyp:

It is an adenomatous polyp in which the stroma is dense and fibrous.

3- Fibroid polyp:

It is firm in consistency. It is attached by a pedicle to the cervical canal or it may arise from the ectocervix. The tip may undergo necrosis and infection and may resemble carcinoma of cervix.

4- Malignant polyp:

Carcinoma or sarcoma including the rare highly malignant sarcoma botryoids (grape-like sarcoma).

5- Bilharzial polyp:

The patient is usually young with a history of bilharziasis as terminal. The polypi are single or multiple and firm in consistency. Biopsy confirms the diagnosis.

6- Tuberculous polyp:

Usually secondary to a tuberculous lesion elsewhere in the body. They are multiple, dark red in colour and soft in consistency.

Recurrent Fibroid

Definition

- **Anatomical recurrence:** Reappearance of new tumors after myomectomy.
- **Symptomatic recurrence:** Persistent or reappearance of symptoms especially menorrhagia.

Etiology:

- **Recurrent fibroid:** (5-10 %)
 1. Development of a new fibroid.
 2. Missed small submucous fibroids or small seedling fibroids.
- **Recurrent bleeding:** (3-5 %).
 1. Recurrent fibroid.
 2. Hormonal imbalance (persistent cause).

Endometriosis & adenomyosis

Definition:

➤ **Endometriosis** is the presence of functional endometrial tissue (glands & stroma) outside the normal uterine cavity "ectopic endometrium".

➤ **Adenomyosis** is the presence of endometrial tissue inside the myometrium.

Prevalence: - 5-10% of adult woman

- 20- 40% of infertile women.

Sites:

(A) Pelvic endometriosis:

- Ovaries "commonest" 60-70%.
- Douglas pouch.
- Uterosacral ligament.
- Rectovaginal septum.
- Broad ligament.
- Uterovesical pouch.
- Vulva, vagina, cervix.
- Rectum & bladder.

(B) Extra pelvic:

- Umbilicus.
- Abdominal scar.
- Viscera: Appendix, Sigmoid colon Lung, pleura.
- Etiology:



Predisposing factors:

- 1] **Age:** 30- 40y.
- 2] **Parity:** Nullipara or low parity.
- 3] **Socioeconomic level:** High socioeconomic standard
- 4] **Race:** White race.
- 5] **Family history:** common in Japaness (certain genes on chromosome 17 are related to pathogenesis of endometriosis).
- 6] **Hyperestrogenism:**
 - Common in women with low parity.
 - It regresses after menopause
 - Commonly associated with endometrial hyperplasia.

7] **Outflow obstruction:** Cervical stenosis, 3rd degree RVF and cryptomenorrhea.

8] **Smoking and exercise:** reduce the incidence of endometriosis (produce hypoestrogenic condition)

Theories: it can be explained by more than one theory.

(1) Tubal regurgitation theory of Sampson:

- Endometrial tissue reaches pelvis by retrograde menstruation. It explains pelvic endometriosis but does not explain other sites.
- It falls 1st on ovary, Next on Douglas pouch "commonest sites".

(2) Serosal metaplasia theory of Meyer & Ivanof:

- Peritoneum & germinal epithelium of ovary have the same embryologic origin of endometrium "coelomic epithelium".
- It may undergo metaplasia into endometrial tissue by abnormal stimulus (hormonal or infection).

(3) Induction or combined theory of Lavender:

- Regurgitation of menstrual blood stimulates coelomic epithelium to undergo metaplasia.

(4) Halban theory:

- Fragments of endometrium spread by lymphatics or veins to reach any parts of the body.

(5) Implantation (Rokitansky) theory:

- Implantation of endometrial tissue may occur in abdominal scar following operation on uterus "myomectomy or C.S."

V. Endometriosis & Adenomyosis

- Also, it may be implanted on vaginal or perineal scar following child birth or curettage.

(6) Immunological theory:

- Failure of immune system to eradicate implanted endometrial tissue (↓ cell mediated cytotoxicity).

(7) Genetic factor:

- There is familial tendency to develop endometriosis.

(8) Tissue injury and repair theory:

- Chronic uterine hyperperistalsis induce microtrauma at the endometrial – myometrial interface with dislocation of fragments of basal endometrium into the peritoneal cavity or the depth of myometrial wall (**the most recent theory**).

N.B.: The ectopic endometrium responds to ovarian hormones → cyclic shedding → reactive inflammatory response & adhesions.

Gross pathology:

Gross pathology includes endometriotic **implants**, endometriotic **adhesions** & **endometrioma**.

Implants:

- **Size:** Variable in size (few millimeters up to 2 cm).

- **Site:** May exist superficially or invade the underlying stroma.

- **Shape:**

a) **Typical:** Bluish gray powder burns or burnt match head.

b) **Atypical:** Non-pigmented, clear vesicles, white plaques, flame-like areas, peritoneal reaction & surface defects.



Adhesions:

a) Variable, from thin filmy adhesions to very thick adhesions obliterating the pelvis (frozen pelvis).

b) Adhesions lead to fixed retroversion of the uterus.

Endometrioma:

Site: More common in the ovary (*bilateral*), but may develop in any location.

Size: variable & may reach 20 cm.

Microscopic picture: it is essential for diagnosis to find:

- 1- Endometrial glands & epithelium.
- 2- Endometrial stroma.
- 3- Haemorrhage.

- The endometrial tissue is usually present in the wall of endometrioma but sometimes, the enclosed fluid destroys the endometrial lining leaving only fibrotic cyst wall infiltrated with hemosiderin laden macrophage.

Symptoms:

- 20% of cases are asymptomatic.

- **Classical triad is:** dysmenorrhea, dyspareunia, infertility.

[1] Pain: (commonest symptom; 80%)

1. Crescendo dysmenorrhea: (progressive dysmenorrhea)

- It starts 3-5 days before menstruation.
- ↑ with menstrual flow due to bleeding in ectopic site.
- Reach maximum at end of menses.
- It gradually ↓ due to absorption of blood.

2. Deep dyspareunia: due to:

- Pelvic adhesions.
- Pelvic congestion.

V. Endometriosis & Adenomyosis

- RVF.

- Endometriosis of rectovaginal septum.

3. Chronic pelvic pain: pelvic adhesions & congestion.

4. Low back pain: - Uterosacral ligament affection.

5. Dyschezia: "painful defecation": (uterosacral ligament - rectovaginal septum).

6. Dysuria: painful micturation (endometriosis of bladder- pelvic congestion).

7. Acute abdominal pain → ruptured chocolate cyst.

[2] Infertility: 30- 40% due to:

1. Ovarian factors:

- Anovulation
- Lutenized unruptured follicle
- Luteal phase defect.

2. Tubal factor:

- Peritubal adhesions:
- Kink of the tube.
- Interfere with ovum pick up.
- PG → ↓ peristalsis & ovum pick up.

3. Uterine factor:

- RVF
- Impaired implantation.

4. Vaginal:

- Dysparunia.

5. Prostaglandins: ↑ in peritoneal fluid (PGF2 α)

- Interfere with ovum pick up & tubal motility.
- Leuteolysis (block LH receptor on corpus luteum).
- Impaired implantation.

6. Autoimmune mechanism:

- Degeneration of ectopic endometrium → Ag → antibody production (auto antibodies → 60% of cases).
- It prevents implantation → infertility or repeated abortion.

7. Hostile peritoneal fluid:

- Macrophages phagocytose sperms.
- Macrophages produce: cytokines, proteolytic enzymes → hostile to gametes.

[3] Other symptoms:

1. Pelvic congestion symptoms: menorrhagia, leucorrhea.

- Menorrhagia:
- Pelvic congestion.
- Hyperplastic endometrium.
- Polymenorrhea: pelvic congestion.

2. Extragenital bleeding at time of menstruation.

- Cyclic hematuria during menstruation.
- Cyclic bleeding per rectum during menstruation.
- Nasal mucosa → epistaxis.
- Stomach → haematemesis.
- lung → hemoptysis.
- Intestine → melena.

3. Bluish nodules → enlarged, painful & tender during menstruation → umbilicus, laparotomy scar, vulva.

. Intermittent pyrexia (absorption of pyrogenic materials from shed endometrium in ectopic sites).

V. Endometriosis & Adenomyosis

Signs:

- Not specific but suggestive.
 - Abdominal: Endometriotic nodules in umbilicus or scars may be seen.
 - Pelvic:

1- **Adnexa:** Tender, cystic, enlarged (ovarian cysts bilateral in 50%).

2- **Uterus:** Fixed RVF.

3- **Douglas pouch & uterosacral ligaments:** Multiple tender nodules.

4- **Vulva, vagina & cervix:** Endometriotic nodules.

Investigations:

1- **Laparoscopy** (the golden investigation in endometriosis):

a) Confirm diagnosis (biopsy).

b) Therapeutic.

2- **Noninvasive techniques:**

a- **Imaging:**

- **Ultrasonography:** Can diagnose endometrioma (especially if its diameter ≥ 20 mm) as a cystic structure with thick wall, thick septations & echogenic wall foci. Color Doppler transvaginal sonography often demonstrates pericystic, but not intracystic flow.
- **MRI** has no advantage over ultrasound in the assessment of endometriomas, but may assist in the evaluation of deep lesions.

b- **Serum CA-125:** Prognostic not diagnostic for follow up of treatment.

3- **Cystoscopy, proctoscopy and sigmoidoscopy:**

→ Endometriosis of urinary bladder & bowel.

Classification: by laparoscopy

- According to **American Fertility Society (AFS)**, Endometriosis has been classified into 4 stages based on site, size of lesions & density of adhesions.

- **Scoring:**

Stage I (minimal)

Stage II (mild)

Stage III (moderate)

Stage IV (severe)

Differential Diagnosis:

- 1- **Ovarian endometriosis** from chronic PID & other ovarian swellings (differentiated by laparoscopy).
- 2- **Douglas pouch endometriosis** from nodules in D.P. (T.B., endometriotic nodules & secondaries).
- 3- **Frozen pelvis** (pelvic endometriosis) from other causes of frozen pelvis.
- 4- **Menuria:** Endometriosis & uterovesical fistula.

Treatment of endometriosis:

- It depends on: severity of symptoms, desire of fertility & extent of disease.

I. Expectant treatment:

- * Indicated in young patient with small lesions & mild symptoms.

* Lines:

- Encourage pregnancy: "management of any factor → infertility" → pregnancy changes endometrium into decidua with subsequent atrophy & regression.
- Symptomatic treatment: anti prostaglandin for pain.
- Follow up every 6 months.

II. Hormonal treatment:

- **Indication:**

1. Young infertile patient with stage 1 or 2 disease.
2. Pre-operative for 6- 12 weeks to make dissection easier.

V. Endometriosis & Adenomyosis

3. After conservative surgery to allow residual lesion to disappear.
4. Recurrence after conservative surgery.
5. When surgery is contraindicated or refused.

- Principle:

- * Ectopic endometrium responds to hormones like normal endometrium.
- * Aim is to cause atrophy of ectopic endometrium by:
 - Pseudopregnancy
 - Pseudomenopause.
 - * Mifeprestone causes atrophy of endometrial tissue.

(A) Pseudo-pregnancy state:

[1] Gestogens (medroxy progesterone acetate):

- **Mechanism of action:** continuous use (6-9 months) → Pseudo pregnancy causing Pseudo decidualization leading to atrophy of endometrium.
- **Dose:**
 - Provera tablet (10- 30mg daily).
 - Depo-provera: 150mg every 3 month for 6-9 month.
 - Dienogest (recently).

- Side effects:

1. Break through bleeding: ttt by conjugated estrogen for short period.
2. Delayed return to fertility.
3. Headache, depression, wt gain.

[2] Combined oral contraceptive pills:

- It has the same mechanism of action of progestin but with no breakthrough bleeding.
- It is used continuously for 6-9 months creating a state of pseudopregnancy with subsequent pseudodecidualisation and atrophy of endometrium.

(B) Pseudo-menopause:

- Inhibition of ovarian function & amenorrhea.

[1] GnRH agonist (analogues):

- It causes pituitary down regulation → medical hypophysectomy.
- Drugs & doses:
 - * Gosereline (Zoladex) 3.6mg S.C. / month.
 - * Triptoreline (decapeptyl) 3.75mg IM/ month.
 - * Busereline (superfact): nasal spray 300-400ug/ t.d.s.
- Side effects:
 1. Menopausal symptoms (hot flushes & vaginal dryness).
 2. Osteoporosis (If > 6 month): can be avoided by add- back therapy.
 3. Expensive.

[2] Danazol:

- Synthetic 3-isoxazol derivative of 17 α ethinyl testosterone.
- Mechanism: It has marked anti-gonadotrophic, moderate anti-estrogenic & anti-progesteronic action with mild androgenic action.
 - Dose: 600- 800mg / day for 6-9 month.
 - Side effects:
 - * Androgenic side effects.
 - * Expensive.

[3] Gestrionone:

- Weak synthetic androgen + anti progesterone.
- Mechanism → like Danazole .
- Side effects → like Danazole.
- Dose: 1.25- 2.5 mg twice weekly for 6-9 month.

V. Endometriosis & Adenomyosis

[4] Gossypole:

- Extracted from cotton plants.
- Used in China for ttt of endometriosis, fibroid, menorrhagia.
- Mechanisms: ↓ FSH & LH → amenorrhea & endometrial atrophy.
- Dose: 20mg orally daily → 2 month. Then 20mg twice weekly for maintenance.

III. Surgical treatment:

[1] Conservative surgery: young patient.

- Indications:

- Serve endometriosis & Failure of medical and hormonal treatment.

- Procedure:

- Adhesiolysis, Excision of chocolate cysts & endometriomata, Correction of retroversion, Fulguration of endometriotic foci, Presacral neurectomy.

[2] Radical surgery:

- Indications:

- Recurrent disease, severe endometriosis, patient completed her family with no response to medical & hormonal treatment.

- Procedure:

- Total abdominal hysterectomy with bilateral salpingo-oophorectomy.

Adenomyosis

Definition: It means the presence of endometrial glands & stroma in the myometrium, with adjacent smooth muscle hyperplasia.

Stromal adenomyosis: is a variant of adenomyosis that is formed only of endometrial stroma (considered a low grade stromal sarcoma).

Epidemiology:

- The estimated incidence is about 10 – 30 %.

It is generally accepted that about 15 % of women will develop adenomyosis in their late thirties & early forties.

- About 15% of patients with adenomyosis have associated endometriosis.

- It is common in:

* Age: 40- 50.

* Multipara.

* High socioeconomic class.

* Smoking: ↓ endometriosis.

Etiology: Cullen diverticular theory

- There is endometrial diverticulum into the uterine wall, then this diverticulum losses its connection to endometrium.

Pathology:

[1] Gross picture:

1) **Localized form:** → More common in posterior wall.

- It simulates fibroid but differentiated by:

* No capsule.

* No whorly appearance.

* Contains blood.

2) **Diffuse form:**

- The whole uterus which undergoes myometrial hypertrophy → symmetrically enlarged, firm, ± 12Wk.

- There may be associated endometrial hyperplasia.



V. Endometriosis & Adenomyosis

[2] Microscopic picture:

- Islands of endometrial glands & stroma are found through the myometrium.
- Hyperplastic changes in the myometrium & endometrium.

Symptoms: 30- 40% of patients are asymptomatic:

1] Menorrhagia: "main complaint" due to:

- ↑ vascularity.
- ↑ surface area of endometrium.
- Impaired myometrial contraction.
- Associated endometrial hyperplasia.

2] Dysmenorrhea: "congestive dysmenorrhea".

3] Pelvic discomfort.

Examination:

1. Uterus is symmetrically (diffuse type) or asymmetrically (localized) enlarged usually < 10 weeks.
2. Uterus is tender during bimanual examination (premenstrually).
3. The adenomatous uterus is usually softer than the myomatous uterus.

Investigations:

- Histopathological examination: after hysterectomy is the only sure diagnosis.

[1] Transvaginal u/s: it may reveal:

- Diffuse echogenecity.
- Myometrial cysts.
- Subendometrial nodules.
- Subendometrial liner striations.
- Asymmetrical myometrial thickening.
- Poor definition of endometrial/ myometrial border.

[2] MRI: Accurate diagnosis.

D.D.: Diffuse form is differentiated from causes of symmetrically enlarged uterus.

Treatment:

[1] Definitive treatment is:

Total abdominal hysterectomy with or without salpingo-oophorectomy.

[2] Palliative treatment (medical & hormonal):

May be indicated if symptoms are tolerable & pregnancy is desired.

Displacements, Urogynecology & Traumatic Anatomical support of genital organs

(1) Endopelvic fascia: It is composed of:

1. Fascial sheaths.
2. Pelvic condensations around extra-peritoneal parts of organs.
3. Cervical ligament: strong condensation of endopelvic fascia surrounding vaginal vault and supravaginal part of cervix.
 - Mackenrodt's ligament.
 - Uterosacral ligament.
 - Pubo cervical ligament.

(2) Pelvic floor:

1. Levator ani muscle.
2. Coccygeus muscle.
3. Pelvic fascia covering them.
4. Perineal muscles.

(3) Anteverted antiflexed position: (AVF)

It prevents sagging down of uterus through vagina.

(4) Other structure that provide minor support:

1. Bony pelvis.
2. Perineal body and perineum.
3. Round ligament, ovarian lig. and broad ligament.
4. Peritoneum and sub peritoneal reticulum.

Genital prolapse

Definition:

Descent of one or more of genital organs below their normal anatomical position.

Etiology :

(A) Predisposing factors (primary causes):

1) Weakness of endopelvic fascia (cervical ligaments):

1. Obstetric trauma: **the commonest cause:**

- Large fetus.
- 1st stage: straining during 1st stage.
- 2nd stage:
 - * Prolonged 2nd stage.
 - * Forceps or breech extraction before full cervical dilatation.
- 3rd stage: downward pressure on uterine fundus.
- Early ambulation and lack of pelvic floor exercise.
- Repeated unspaced pregnancies.

2- Congenital weakness: virginal and nulliparous prolapse:

- Commonly associated by spina bifida.
- It may be accompanied by generalized visceroptosis.

3- Post-menopausal atrophy: appearance of prolapse after menopause.

2) Weakness of pelvic floor muscles:

- 1- As a result of repeated successive vaginal deliveries.
- 2- Un-repaired or badly repaired perineal tear or hidden perineal tear.
- 3- More with 2nd degree perineal tear.
- 4- ↓ innervation of levator ani in case of spina bilida occulta.

VI. Displacements, Urogynecology & Traumatic

3) RVF: (1st degree):

It brings longitudinal axis of uterus with that vagina.

(B) Precipitating factors (2ry causes):

These cause prolapse when a weakness is already present.

1) ↑ intra abdominal pressure:

- Chronic cough, constipation.
- Ascitis, abdominal tumors and obesity.

2) ↑ wt of the uterus:

- Small fibroid.
- Early pregnancy.
- Subinvolution.
- If the size of the uterus is large, it rests on the pelvic brim and will not prolapse.

3) Traction on uterus: by large cervical polyp or vaginal prolapse.

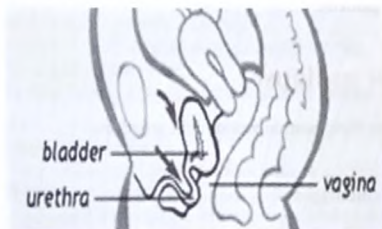
Classification of genital prolapse:

(1) Anatomical classification:

Vaginal prolapse

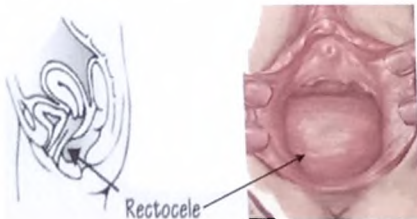
1- Anterior vaginal wall prolapse:

- Descent of upper part of ant. Vaginal wall + base of bladder → **Cystocele**.
- Descent of lower part of ant. Vaginal wall + urethra → **Urethrocele**.
- Descent of all ant. Vaginal wall → **Cysto-urethrocele**.



2- Posterior vaginal wall prolapse:

- **Rectocele:** descent of lower 2/3 of posterior vaginal wall with anterior rectal wall.
- **Enterocele:** descent of upper 1/3 of post. Vaginal wall + peritoneal sac from Douglas pouch containing intestine "**Hernia Douglas Pouch**".



3- Vault prolapse: descent of vaginal vault after hysterectomy.

VI. Displacements, Urogynecology & Traumatic

Uterine prolapse

- 1st degree:** The external os descend below level of ischial spine but does not protrude outside vulva on straining.
- 2nd degree:** The cervix but not the whole uterus protrudes outside vulva on straining (incomplete procidentia)
- 3rd degree:** The whole uterus protrudes outside vulva on straining and vaginal wall completely inverted over it → Complete procidentia



Combined prolapse

(1) Utero-vaginal prolapse:

Descent of uterus followed by the vagina. It usually occur in nulliparous prolapse (weakness of cervical ligaments).

(2) Vagino-uterine prolapse:

Descent of vagina followed by uterus. It usually occurs in cases due to obstetric trauma (weak pelvic floor).



Secondary changes:

(1) The vagina:

Inversion and exposure of vagina leads to:

- Thickening of the wall due to odema and congestion.
- Mucosa loses its rugae and become smooth.
- Keratinization and pigmentation.
- Trophic ulcers (decubitus ulcer): due to:
 - Chronic congestion.
 - Friction with patient thighs or cloths.
 - Irritation by urine and faeces
 - Post-menopausal atrophic changes.



(2) The cervix:

1- **Hypertrophy** due to congestion and edema (chronic hypertrophic cervicitis).

2- **Trophic ulcer.**

3- **Supravaginal elongation:** in case of vaginouterine prolapse, vaginal vault applies traction on cervix, while stronger upper point of Mackenrodt's ligament which is attached to supravaginal portion resists traction.

4. Sometimes the prolapsed cervix and adjacent vaginal walls become congested and oedematous and cannot be reduced by the patient i.e. **incarcerated**.

(3) The uterus:

- Descent of uterus leads to congestion (menorrhagia- leucorrhoea).
- In 2nd and 3rd degree uterine prolapse → uterus is retroverted.

(4) Tubes and ovaries:

Descend with prolapse of uterus → congestion → dyspareunia and polymenorrhea.

(5) Urinary tract:

1- There is **descent of the base** of the bladder leading to difficulty of micturition (dysuria). Sometimes, the patient cannot micturate unless she pushes up the cystocele with her finger in the vagina.

- Descent of bladder base: residual urine → irritation and cystitis.

VI. Displacements, Urogynecology & Traumatic

- 2- **Bladder neck:** descent bladder neck and stretch of internal urethral sphincter → stress incontinence.
- 3- **Urethra:** kink of urethra:
- Dysuria.
 - Urine retention.
 - Mask already present stress incontinence.
- 4- **Ureter:** kink in case of 3rd degree ut. Prolapse → hydroureter and hydronephrosis.
- (6) **Rectum:** Sense of in complete act of defecation.

Diagnosis of prolapse:

Symptoms:

Minor degrees of prolapse are **asymptomatic**.

- (1) **Sensation of heaviness** in pelvis due to presence of swelling in the vagina.
- (2) **Swelling** which fills vagina or protrudes from the vulva on standing or straining and disappear on lying down.
- (3) **Low backache:** due to:
- Stretch of uterosacral ligament.
 - Pelvic congestion.
 - ↑ by the end of the day.
 - It may be absent in 3rd degree uterine prolapse → due to damage of nerves by marked stretch of uterosacral ligament.
- (4) **Pain in groin:** due to stretch of round ligament.
- (5) **Urinary symptoms:**
- Difficulty on micturition: inability to complete micturition unless mass is pushed upwards by fingers in vagina.
 - Frequency of micturition:
 - Diurnal → irritation of trigone.
 - All the time → cystitis.
 - Stress incontinence.
 - UTI: fever, rigors, loinc pain.
- (6) **Rectal symptoms:**
- Difficulty in defecation and patient needs to reduce the mass to complete defecation.
 - Heaviness in rectum.
 - Piles: congestion, straining and congenital weakness.
- (7) **Symptoms of pelvic congestion:**
- Menorrhagia.
 - Congestive dysmenorrhea.
 - Leucorrhea (↑ vaginal discharge).
 - Trophic ulcer may cause a purulent or blood stained vaginal discharge.
- (8) **Dyspareunia:**
- Due to presence of swelling in vagina or pelvic congestion.
- (9) **Infertility (rare):** due to:
- Dyspareunia.
 - Cervicitis.
 - Congested endometrium → prevent implantation.

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- RVF.
- Kink of tube.
- Ovarian congestion.

(10) Symptoms of enterocele:

- May be asymptomatic.
- Heaviness in the pelvis.
- Vulval swelling.
- Low backache.
- Dyspareunia due to the presence of a swelling in the vagina.

Signs:

(1) General examination:

- 1- Exclude obesity.
- 2- Chest exam: chronic bronchitis.
- 3- Back → spina bifida (tuft of hair, lipoma).
- 4- Lower limbs → varicose vein, flat foot (weakness of mesenchyme).

(2) Abdominal examination:

- 1- Renal angle → hydronephrosis, pyelonephritis → tenderness.
- 2- Visceroptosis → nulliparus prolapse.
- 3- Associated hernia.
- 4- ↑ intra abdominal pressure → ascitis.

(3) Local examination:

Inspection: Ask the patient to cough or strain to detect:

- 1- Type of prolapse:
 - Uterine: external os is seen in 2nd and 3rd degree ut. Prolapse.
 - Vaginal: ant. and post. wall prolapse.
- 2- Secondary changes (trophic ulcers).
- 3- Stress incontinence.
- 4- Perineum is inspected for lacerations.

Palpation:

1- Type of prolapse:

- Vaginal:
 - Cystocele.
 - Urethrocele.
 - Rectocele.
 - Enterocele.
- Uterine:
 - 1st degree ut. Prolapse (by P/V).
 - 2nd and 3rd degree: finger test.

2- Examine tone of levator ani:

Grasp levator ani with middle and index finger in vagina and thumb on perineum and feel tone of muscle and ask patient to contract pelvic floor "Levator test".

3- Bimanual examination → uterus and adnexa.

4- P/R: D.D. rectocele from enterocele.

Speculum examination:

- 1- Sim's speculum in left lateral position.
- 2- Sound: Supra-vaginal elongation.

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Management:

(A) Prophylaxis:

1- During labor:

- Avoid straining in 1st stage.
- Avoid forceps application or breech extraction before full cervical dilatation.
- Avoid repeated downward pressure on uterus during third stage.
- Frequent emptying of bladder.
- Episiotomy when indicated.

2- After labor:

- Any perineal tear should be sutured immediately.
- Pelvic floor exercise.
- Treatment of cough and constipation.
- The patient is asked to lie on her abdomen for one hour daily to prevent retroversion which predisposes to prolapse
- If prolapse is detected during the puerperium, a ring pessary is applied for 3 months until the supporting ligaments involute and restore their tone.
- Proper spacing of pregnancies.

3- During hysterectomy:

- The stumps of the round, cardinal and uterosacral ligaments are sutured to the vault of the vagina to prevent its prolapse.

(B) Pelvic floor exercise:

- Simple pelvic floor exercise: ask the patient to contract the levator ani repeatedly for 2 minutes twice daily over a number of months.
- Kegel's perniometer: A pneumatic tube is inserted into the vagina, and the woman contracts the levator ani muscles to raise the pressure in the connected pressure gauge to the maximum.
- Vaginal cones.
- Electrical stimulation.

(C) Pessary (palliative) treatment:

Pessary does not cure prolapse. It only keeps the uterus up and provides temporary relief of symptoms.

Indication:

- Prolapse of uterus in early pregnancy → till 20th week.
- Prolapse detected in puerperium.
- Slight degree of prolapse in young patient till she completes her family.
- To help healing of trophic ulcer.
- Unfit for surgery → very old or in heart failure.
- Refuses surgery.

Types of pessary:

[1] Ring pessary:

- Made of rubber or plastic.
- It is introduced above level of levator ani.
- It stretches vaginal walls → prevent descent of uterus.

[2] Cup and stem pessary: (Napier) not used nowadays

Used in cases with very weak or lacerated levator ani.



VI. Displacements, Urogynecology & Traumatic

Precautions during wearing pessary:

- Daily vaginal douche by saline.
- Every month: pessary is removed and vagina is examined for ulceration. Then pessary is reapplied.
- It stretches tissues and after few months (4-6 m) it needs to be changed (bigger size) to control prolapse.
- Removed if there is: pain, bleeding, offensive discharge.

Complications:

- Irritation: leucorrhea, vaginitis "rubber pessary".
- Ulceration: bleeding, offensive discharge.
- If neglected: vesicovaginal fistula.

(D) Surgical treatment:

Timing:

- Post-menstrual to (↓ bleeding- exclude pregnancy).
- 3-6 months after labor or abortion → involution of tissue.
- 3-6 months after any attempt of repair.

Pre-operative preparation:

- CBC and correction of anemia or diabetes.
- Treatment of chronic cough or constipation.
- Weight reduction in obese patients.
- Urinary tract:
 - Urine analysis and culture and sensitivity with treatment of any infection.
 - Kidney function tests in 3rd degree uterine prolapse.
- Trophic ulcers:
 - ↓ congestion by reducing prolapse in place → vaginal pack soaked with flavine solution or ring pessary.
 - Estrogen → to help healing of epithelium "specially post-menopausal".
 - Silver nitrate painting → if slow healing.

Choice of operation: It depends on:

- Age and parity of patient.
- Type and degree of prolapse.
- Etiology.
- Presence of complications.

[1] Vaginal prolapse

Rectocele: → posterior colpo-perineorrhaphy.

Cystocele: → anterior colpoorrhaphy or classical repair.

- Post colpoperineorrhaphy is added to:

→ To strengthen the pelvic floor to prevent recurrence.

Cysto-rectocele: → classical repair.

= (anterior colpoorrhaphy + posterior colpoperineorrhaphy).

Enterocoele:

1- Vaginal repair:

- Incision of posterior vaginal wall.
- Dissection of mass from vaginal wall.
- Sac is opened, contents are reduced and the sac is excised.
- Suturing uterosacral ligaments (culdoplasty).

VI. Displacements, Urogynecology & Traumatic

2- Abdominal repair:

- Douglas pouch is closed by series of purse- string sutures from below upwards.
- Sutures pass through: post- wall of cervix ,uterosacral ligament and serous coat of rectum – **Moschowitz operation.**
- If sutures pass only in peritoneum of Douglas pouch → **Halban's operation.**

Vault prolapse:

- Vaginal repair (transvaginal sacrospinus colpopexy): suturing vault to sacrospinus ligament.
- Abdominal repair (abdominal sacral colpopexy; sling operation): suturing vault to periosteum of sacrum.



[2] Uterine prolapse:

Nulliparas prolapse:

- o Abdominal sling operation → cervico- sacropexy.

Combined uterovaginal prolapsed in young patients:

- o If with supravaginal elongation of cervix: → fothergill - Manchester operation.
- o If no supra vaginal elongation: → modified fothergill's.

Around and after menopause:

- o Vaginal hysterectomy and pelvic floor repair: It consists of anterior colporrhaphy + suturing cardinal ligaments to vaginal vault+ post. Colpoperineorrhaphy.
- o Le-Fort's operation:
 - If patient unfit for surgery and sexually inactive.
 - Rectangular flap is excised from anterior and posterior vaginal wall and raw area are sutured together but leaving 2 small channels on either side to allow drainage of any cervical discharge.

Pelvic Organ Prolapse Quantification System (POP-Q)

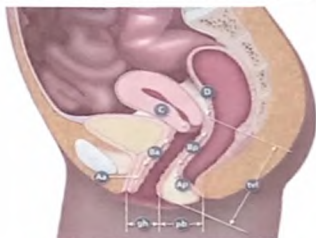
It is an objective system to describe and stage POP by measuring various points

- The hymenal ring was selected as a reference point.
- There are 9 site- specific measurements:
 - 1- Point Aa: 3cm from hymen ring anteriorly.
 - 2- Point Ap: 3cm from hymen ring posteriorly.
 - 3- Point Ba: point of maximum prolapsed on the anterior vaginal wall.
 - 4- Point Bp: point of maximum prolapsed on the posterior vaginal wall.
 - 5- Point C: cervix or vaginal cuff after hysterectomy.
 - 6- Point D: Douglas pouch (post. Fornix).
 - 7- Genital hiatus: middle of urethral meatus to posterior midline hymenal ring.
 - 8- Perineal body: post margin of genital hiatus to middle of anal opening.
 - 9- Total vaginal length: greatest depth of vagina with vaginal apex reduced to full normal position.
- The anatomical position of the 1st 6 points is measured in centimeters:
 - Proximal to hymenal ring (-ve number).
 - Distal to hymenal ring (+ve number)
 - With the plane of hymenal ring → zero.

VI. Displacements, Urogynecology & Traumatic

Stages of pelvic organ prolapse:

| | |
|---------|--|
| Stage 0 | No prolapse is demonstrated. |
| Stage 1 | The most distal portion of the prolapse is >1cm above the level of the hymen. |
| Stage 2 | The most distal portion of the prolapse is <1cm proximal or distal to the plane of the hymen. |
| Stage 3 | The most distal portion of the prolapse is >1cm below the plane of the hymen but not further than 2 cm less than the total vaginal length. |
| Stage 4 | Complete eversion of the vagina. |



Pelvic organ prolapse quantification six sites (points Aa, Ba, C, D, Bp and Ap), genital hiatus (gh), perineal body (pb) and total vaginal length (tvL)

Simplified POP-Q

| | | |
|---|--|---|
| Aa Descent of fixed point on anterior wall | Ba The lowest part of the upper anterior vaginal wall | C The lowest part of the cervix |
| GH Genital Hiatus | PB Perineal Body | TVL Total vaginal length |
| Ap Descent of fixed point on posterior wall | Bp The lowest part of the upper posterior vaginal wall | D Vault or insertion uterosacra |

VI. Displacements, Urogynecology & Traumatic

Differential diagnosis of mass protruding from vulva

1) From anterior vaginal wall:

[1] Cystocele:

- Appears on standing or straining.
- It is reducible (can be moved from its position) and compressible.
- If a catheter is passed it can be felt in the mass.

[2] Gartner cyst:

- Anterolateral wall. - Non compressible and irreducible.
- Catheter in normal direction (anterior to the cyst).

[3] Urethral or bladder diverticulum:

- Compressible and pressure on diverticulum → discharge pus or urine from external urethral meatus.
- Urethroscope and cystoscope will show opening of the diverticulum.

[4] Skene's tubule cyst:

- Firm cyst in lower part of anterior vaginal wall.
- Non compressible.

2) From posterior vaginal wall:

[1] Rectocele:

- Appears on standing or straining. - Reducible and compressible.
- A finger in the anus will pass into the mass.

[2] Enterocele (hernia of Douglas pouch):

- It arises from upper part of posterior vaginal wall.
- Impulse on cough. - Gurgling sensation.
- P/R → rectum is pushed backwards by the swelling and not forming part of it.
- **Malpus test:** combined P/V and P/R in standing position to differentiate enterocele and rectocele (thumb in the vagina and index in rectum). In case of enterocele intestine separate both fingers on straining.

[3] Rectocele: from dermoid cyst:

- Non-compressible and irreducible. - P/R does not pass into mass.

3) From the uterus:

[1] 1- 2nd and 3rd degree uterine prolapse:

- The external os appears from the vagina.
- They are differentiated by: finger test or grip sign:
 - **2nd degree:** The fingers cannot be approximated at vulva because only part of uterus that protrudes outside vulva and therefore → uterus is felt between examining fingers.
 - **3rd degree:** Fingers can be approximated at base of prolapsed mass (vulva) → as the whole uterus is prolapsed outside vulva.

[2] Congenital elongation of portio vaginalis (false prolapse)

- Vaginal vault at normal level (ischial spine).
- Vaginal fornices are deep (palpation- sounding).
- Treated by amputating the elongated portio vaginalis leaving a normal length of the cervix.

[3] Fibroid polyp:

- Absence of external os.
- Cervix at normal level with the pedicle of the tumour coming out through the cervix;
- Sound is introduced for long distance in uterine cavity.



VI. Displacements, Urogynecology & Traumatic

[4] Inverted uterus:

- Absence of external os.
- The mass is covered by smooth endometrium;
- Ut. Not felt abdominally.
- Sound pass for short distance or cannot pass.

[5] Cauliflower carcinoma or sarcoma of the cervix:

- Friable, necrotic, indurated and bleeds on touch.

Recurrent prolapse

Definition:

- It is descent of genital organs after previous repair.
- The rate of recurrence is about 7%.

Causes:

1) Causes before operation:

- Congenital weakness of the cervical ligaments.
- Bad general health and anaemia.
- The presence of infection or ulceration in the cervix or vagina.
- If the factors which increase the intra-abdominal pressure as chronic cough, chronic constipation, and obesity are not corrected before operation.

2) Causes during operation:

- Poor surgical techniques.
- Bad choice of operation, e.g., vaginal repair for a congenital uterine prolapse.
- Missing a hernia of Douglas pouch (commonest cause).
- An elongated cervix which was not amputated.
- Shortening of vaginal wall, so the cervix becomes near to the vaginal orifice.
- Use of early-absorbable sutures leads to recurrence.

3) Causes after operation:

- Infection.
- Early ambulation.
- Early subsequent pregnancy.
- Repeated deliveries.
- If episiotomy is not done at the time of subsequent delivery.
- Postmenopausal atrophic changes.

Clinical Picture:

- History of previous operation for repair of prolapse.
- Presence of symptoms which depend upon the type of prolapse.
- Examination reveals the nature of prolapse, and scar of previous operation.
- The cause of recurrence has to be determined as chronic cough and obesity.

Treatment:

- Treat the cause of recurrence.
- The operation depends upon the type of prolapse and patient general condition.
- Operation is done at least 3-6 months after the previous repair to allow absorption of scar tissue. Fibrous tissue resulting from the previous operation makes the second operation more difficult.
- Use of synthetic mesh is common.

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Anatomy of anterior vaginal wall:

- On either side of urethral meatus there is a depression → parameatal recess.
- Submetalar sulcus: 0.6cm from external urethral meatus.
- Transverse vaginal sulcus: transverse groove 3 cm from urethral meatus → at junction of urethra with the bladder neck.
- Bladder sulcus at level of fundus of bladder, 4 cm from the transverse sulcus.

Relationship between uterine prolapse and cervical carcinoma (theoretical):

- Third degree uterine prolapse predisposes to vaginal carcinoma. However, it is very rare to find cervical carcinoma in association with complete procidentia.
- This may be explained by:
 - Congestion of the cervix and keratinization of the covering cervical epithelium may raise the resistance to cancer.
 - The prolapsed cervix is not bathed in any irritating vaginal discharge.
 - The presence of the cervix outside the vagina decreases its temperature. It is known that the undescended testicles which lie in a warm place inside the body are more liable to develop cancer.
 - Infiltration of the parametrium in case of cervical carcinoma fixes the uterus and prevents its descent.

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Inversion of the Uterus

Definition:

The uterus is totally or partially turned inside out.

Types:

- Acute inversion: complications of 3rd stage of labor.
- Chronic inversion: gradual prolapse of the uterine fundus through the dilated cervix.

Degrees:

- 1st degree: depression of fundus into uterine cavity but not pass through cervix "cupping of fundus".
- 2nd degree: inverted fundus pass through cervix into vagina.
- 3rd degree: whole uterus is inverted and appears at the vulva.

N.B.: The first and second degrees are incomplete inversion, while the third degree is called complete inversion.

Aetiology of chronic inversion:

- **Chronic puerperal inversion:** The uterus undergoes inversion at time of delivery and pass unrecognized.
- **Fundal myoma:** The weight drags down the fundus.
- **Senile inversion:** It occurs in old age due to cervical and uterine atony.

Symptoms:

- **Vaginal discharge.**
- **Contact bleeding or irregular uterine bleeding** due to ulceration or infection.
- **Chronic pelvic pain** due to the presence of tubes and ovaries in the uterine cup.
- **Dyspareunia.**
- **Infertility** because of dyspareunia and infected endometrium.
- **Mass protrudes through vulva.**

Signs:

[1] Abdominal examination:

- 1st and 2nd degree → cupping of the fundus.
- 3rd degree → uterus is not felt.

[2] Vaginal examination:

- In 2nd and 3rd degree → large mass covered by dark red endometrium.
- Sound: → Can not be passed through CX (3rd degree).
→ Passed for short distance (2nd degree).

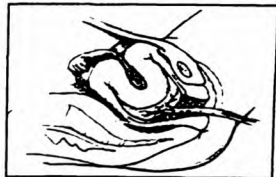
Differential diagnosis:

- Fibroid polyp:
 - Abdominal examination: uterus is felt and enlarged (multiple fibroid).
 - Sounding: sound pass for long distance inside ut. cavity.
- Uterine prolapse.
- Cauliflower carcinoma or sarcoma of vagina and cervix.

Management:

[1] Pre-operative treatment:

- Treatment of infection.
- Repeated antiseptic vaginal douch. - Daily sterile vaginal pack.



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[2] Senile inversion: treated by hysterectomy.

[3] Inversion due to fundal Fibroid:

- Young patient: vaginal myomectomy and correction of inversion.
- Old patient or completed her family: vaginal hysterectomy.
- if malignant tumor: Treatment according to stage.

[4] Chronic puerperal inversion:

(A) Conservative treatment:

- If patient is unfit for surgery.
- Avelling S-shaped reposition.

(B) Surgical treatment:

| Abdominal operations | Vaginal operations |
|---|---|
| 1- Huntington operation: Traction on depressed fundus by vulsellum. | 1- Spinelli's operation: Division of constriction ring anteriorly correction of inversion. |
| 2- Dobbin's operation: Division of constriction ring anteriorly and pulling fundus by vulsellum. | 2- Kustner's operation: Division of constriction ring posteriorly and correction of inversion. |
| 3- Haultain operation: Division of constriction ring posteriorly and pulling the fundus. | 3- Vaginal hysterectomy: Patient >40 y. |
| 4- Abdominal hysterectomy: Patient > 40y. | |

Retroversion and Retroflexion (RVF)

Retroversion: the cervix is bent posteriorly over vagina.

Retroflexion: the body of uterus is bent posteriorly over the cervix.

Causes:

1) Developmental (15%):

The uterus may be normal in size or hypoplastic.

2) Acquired:

1- **Puerperal retroversion:** "Commonest acquired cause"

- Laxity of ligaments of uterus.
- ↑ uterine weight.
- Persistent distension of bladder.
- Prolonged lying in dorsal position.

2- **Pelvic lesions:**

- A tumour lying in front of the uterus pushes it backwards.
- The uterus may be pulled backwards by adhesions as in cases of endometriosis and chronic salpingo oophoritis.

3- **Prolapse:**

As the uterus descends it lies along the axis of the vagina so it becomes retroverted. So retroversion predisposes to prolapse or when the uterus descends it becomes retroverted.

Degrees:

- 1st degree: fundus is directed towards sacral promontory.
- 2nd degree: fundus is directed towards sacral concavity.
- 3rd degree: fundus is directed towards tip of sacrum.



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Types:

- Mobile.
- Fixed.

Symptoms: 50% of cases are asymptomatic.

A- Symptoms due to pelvic congestion:

- Congestive dysmenorrhea, menorrhagia, polymenorrhea, leucorrhea.

B- Symptoms due to abnormal position:

1. Low back pain: pressure of uterus on the uterosacral ligaments and pelvic congestion.
2. Spasmodic dysmenorrhea.
3. Dysparunia: congested ovaries in Douglas pouch.
4. Infertility:
 - Cervix "external os" → away from semen pool.
 - Congestion of endometrium.
 - Kink of tube.
 - Pelvic adhesions.
 - Dysparunia.
5. Complications with pregnancy.
 - Abortion.
 - Incarceration.
 - Anterior sacculation.

Signs: "Vaginal examination"

1. P/V: feels posterior lip of cervix first.
2. External os is directed downwards and forwards or forwards only.
3. On Bimanual examination:
 - Fundus of uterus is felt through posterior fornix not through anterior.
 - The tubes and ovaries are frequently prolapsed in Douglas pouch.
 - The ovaries will be felt as round, mobile, usually tender bodies.
4. Uterine sound: determines position of uterus when bimanual exam. is difficult (obesity).
5. Ultrasound → diagnosis of the case.

Pessary test:

- It is done to determine whether symptoms are due to RVF or other cause.
- Correction of retroversion and maintain normal position by pessary and reexamine after 1 month.
- If symptoms persist → thus symptoms are due to other cause.
- If symptoms disappear and recur when pessary is removed → thus symptoms are due to RVF.

Treatment:

[1] Prevention: proper post partum care:

- Frequent emptying of bladder.
- Patient lie on her abdomen 1h/ day.
- Pelvic floor exercise.
- If puerperal retroversion → pessary for 3 months.



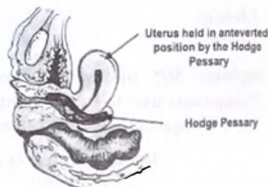
[2] Palliative (pessary) treatment: **Hodge or Smith pessary.**

- The uterus is corrected bimanually and pessary is introduced.
- The pessary is introduced → broad part in posterior fornix → causes traction on uterosacral ligament and narrowing of Douglas pouch.

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* Indications of pessary:

- 1- Pessary test.
- 2- Puerperal retroversion.
- 3- Early pregnancy: if it causes recurrent abortion → >14 wk.
- 4- Contraindication of surgery
- 5- Patient refuses surgery.



[3] Surgical treatment: Symptomatic cases only.

- No symptoms = No treatment.
- The main indication for surgical treatment is dyspareunia caused by prolapse of ovaries in Douglas pouch.
- Also operation is done as an added step to another operation as myomectomy.

* Operations:

- 1- **Modified Guillian's operation:** laparotomy is done and round ligament is shorted by suturing to anterior rectus sheath.
- 2- Retroversion with prolapse: suturing mackenrodt's ligaments together in front of cervix.
- 3- **Added step to another operation (myomectomy):**
 - Plication of round ligament.
 - Plication of uterosacral ligament.

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Incontinence of Urine

It is involuntary escape of urine.

[1] True incontinence:

- It is continuous passage of urine by day and night (not through the urethra).
- It is due to:
 - 1- urinary fistulas.
 - 2- Ectopia vesicae.

(A) Complete incontinence:

- Continuous passage of urine by day and night from vagina.
- No urine is retained in the bladder → no desire to micturate.

Causes:

1. Low, large vesico-vaginal fistula.
2. Bilateral ureteric fistula.

(B) Partial incontinence:

- Continuous passage of urine by day and night from the vagina.
- Some urine is retained in the bladder → patient will have desire to micturate.

Causes:

1. Small, high or valvular v.v. fistula.
2. Unilateral ureteric fistula.

[2] Stress incontinence (sphincteric):

- Escape of few drops of urine through the urethra with increased intra-abdominal pressure (coughing, laughing, sneezing and sudden movement).
- Cause: weakness of sphincteric mechanism at urethrovesical junction.

[3] Urge incontinence (detrusor overactivity, instability):

- The patient feels desire to micturate and large amount of urine passes through the urethra involuntary on her way to W.C.
- Cause: It is due to irritability of bladder → patient cannot inhibit it (e.g. cystitis and neurological lesion).

[4] False incontinence (retention with overflow):

- The urine escapes from the over distended bladder due to chronic retention through urethra.
- Cause: Spinal cord lesion as tabes dorsalis or paraplegia.

[5] Nocturnal enuresis:

- Passage of urine through urethra during sleep.
- Causes:
 - * Children.
 - * Psychological disturbance.
 - * Spina bifida.

Physiology of micturition:

Normally:

- Intravesical pressure at rest is 2-8 cm H₂O
- Intraurethral pressure at rest 100-120cm H₂O
- Thus intraurethral pressure > intravesical pressure
- → maintains continence except during micturition.

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When urine volume: Reach 200 ml → initiate desire to micturate with **no rise** of intravesical pressure.

Control of micturition:

1. Sympathetic: contraction of sphincter + relaxation of detrusor muscle.
2. Parasympathetic: relaxation of sphincter + contraction of detrusor muscle.
3. CNS control: it controls the autonomic N. System.
 - Inhibitory impulses from higher centers if unfavorable condition.
 - Facilitatory impulses, if favorable conditions → voiding.
 - **When urine volume:** reaches 400- 600ml → the desire cannot be restricted → micturition.

Factors maintaining continence at rest:

- (1) Urethral closing pressure (100-120 cm H₂O) > vesical pressure (2-8 cm H₂O).
 1. Urethral mucosal resistance (maintained by internal sphincter and urogenital diaphragm).
 2. Perourethral vascular plexus (4- 6 mmHg) under effect of estrogen.
 3. Bladder neck and upper part of urethra lies above the level of pelvic floor: ↑ intra abdominal pressure → close upper urethra.
- (2) External urethral sphincter + pubococcygeus muscle → 2nd line defence.
- (3) Posterior urethrovesical angle "functional"
 - At rest 100° and During micturition 180.
 - Angle between urethra and vertical line (At rest < 30°C and during micturition >30°C).
- (4) Urethral length: if < 1cm → incontinence.

Factors maintaining continence at stress:

Two synchronous actions → kink of urethra → maintain continence:

1. The bladder neck is pulled upward and forward behind symphysis pubis.
2. Bladder base is pushed downwards and backwards.

Stress incontinence

Definition:

Involuntary escape of few drops of urine though urethra with ↑ intra-abdominal pressure (coughing, sneezing, straining....).

Prevalence:

- It ranges between 10% to 60%.
- It is the commonest cause of urinary leakage.

Degree:

- Grade I: Incontinence with sever stress (coughing, sneezing, jogging).
- Grade II: Incontinence moderate stress (rapid movement, walking up or down stairs).
- Grade III: Incontinence on mild stress → standing. The patient is continent on supine position

Causes:

- Congenital weakness of internal urethral sphincter. Seen in young nullipara.
- Traumatic: obstetric trauma "repeated child birth" → **the commonest cause** of stress incontinence.
- Post-menopausal weakness or atrophy of bladder neck support.
- Genital prolapse: bladder neck below the level of pelvic floor.
- Pregnancy and continuous administration of oestrogen-progesterone to induce pseudopregnancy state to treat endometriosis: progesterone → relaxant and weakness of ligaments and sphincter.
- Congenital defects as short urethra (less than 1 cm).

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N.B. Types of stress incontinence:

- 1- Genuine stress incontinence: pressure equalization stress incontinence with intact neurological and urinary system.

In Genuine S.I.:

- Intraurethral pressure > intravesical pressure at rest
 - During \uparrow intra abdominal pressure $\rightarrow \uparrow$ intravesical pressure = intraurethral pressure \rightarrow painless escape of urine "pressure equalization SI"
- 2- Detrusor instability (overactivity): involuntary contraction of detrusor muscle due to neurological lesion or urinary tract infection.
 3. Mixed.

Diagnosis of stress incontinence:

History:

- Differentiates between different types of incontinence.
- Can detect cause: post-menopausal, obstetric trauma.
- History of vaginal repair or neurological disease.

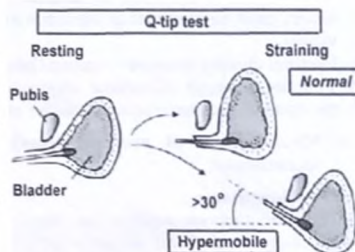
Examination (diagnostic tests):

1. Stress test:

- Bladder is moderately full (200cc).
- Lithotomy position and two labia are separated and patient is asked to cough:
 - Urine escapes \rightarrow incontinent.
 - No urine escapes \rightarrow repeat the test with the middle and index finger press on levator ani \rightarrow if no urine escapes \rightarrow repeat test in standing position and two legs are apart.

2. Cotton swabs (Q. tip) test:

- Patient lies in lithotomy position.
- Q.tip application is applied till the bladder neck.
- Angle between application and horizontal line is measured.
- Patient is asked to strain (Valsalva maneuver) \rightarrow descent of bladder neck and upward movement of applicator \rightarrow measure the new angle.
- Normally: change of angle is less than 30° .
- If change $>30^\circ$ \rightarrow poor support of bladder neck $>90\%$ of cases "urethral hyper-mobility".



A Q-tip cotton swab is placed in the urethra to the excursion with Valsalva (straining), then hypermobility is present

In cases of prolapse:

1. Bonney's test: "In cases of prolapse + stress incontinence"

- o **Aim:** to determine whether the cause of incontinence is descent of bladder neck or weakness of sphincter.
- o **Technique:** index and middle finger put inside the vagina on sides of urethra \rightarrow elevate bladder neck upward.
- o **Ask patient to strain:**
 - * No incontinence \rightarrow it is due to descent of bladder neck \rightarrow repair of prolapse only.
 - * Still incontinent \rightarrow weakness of sphincter \rightarrow repair of prolapse + Kelly's suture.

2. Youssef test: "In cases of prolapse without stress incontinence"

- o **Aim:** to determine hidden incontinence in cases with negative stress test.
- o **Technique:** correct prolapse by 2 fingers or ovum forceps.

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○ Ask patient to strain:

- * Urine escapes → Masked incontinence → repair of prolapse + Kelly's suture.
- * No urine escapes → no incontinence → repair of prolapse only.

Investigations:

1. Urine analysis, culture and sensitivity: → to exclude cystitis.
2. Cysto-urethrography: radio-opaque dye injected into bladder.

On straining:

- Lateral view: Loss of posterior urethrovesical angle > 90° of case.
- A.P. view: Funnelling of bladder neck.
- It may be recorded on video tap "video cysto-urethrography".

3. Cysto-urethroscopy: to exclude lesions of bladder and urethra.

- The bladder neck is examined. It should close in response to straining. However, it opens in case of stress incontinence.

4. Urodynamic studies:

a. Cystometry:

- Measure intravesical pressure while it is being filled with saline.
- To differentiate stress incontinence and detrusor overactivity.
- The most accurate test to diagnose detrusor overactivity.

b. Measurement of urethral pressure:

- To maintain continence, the urethral pressure (100-120 cm water) must be higher than the intravesical pressure (2-8 cm water).
- Urethral closing pressure = urethral pressure - intravesical pr.
- Functional length of urethra: length of urethra along which the urethral pressure exceeds bladder pressure.

c. Measurement of urethral length: <1 cm → stress incontinence.

d. Uroflowmetry:

- The patient sits on uroflow chair and starts to void.
- Normally: voids 20ml/ second and the bladder is emptied in < 20 seconds.
- It is used to evaluate patients with stress incontinence before surgery to exclude difficulty in voiding which may be increased by bladder neck surgery.

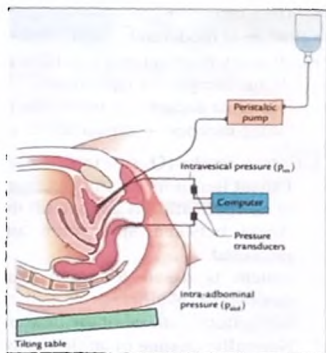
5. Ultrasonography:

- Funnelling of bladder neck (during rest- at stress).
- Diverticulum of bladder and urethra.
- 3-D transvaginal U/S → internal urethral sphincter.

Management:

Prophylaxis:

- 1- During labor: keep bladder empty.
- 2- Episiotomy if necessary.
- 3- Pelvic floor exercise after labor. It includes repeated stoppage of the urinary stream during micturition and repeated contractions of the pelvic floor muscles.



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Conservative (non-surgical treatment):

Indications:

1. Mild stress incontinence.
2. Patient not completed her family as vaginal delivery may damage a bladder neck repair.
3. Unfit for surgery.
4. Associated detrusor over activity "treatment at 1st".

Conservative treatment includes:

[1] Pelvic floor exercise:

- Kegel's perinometer.
- Vaginal Cones.
- Electrical stimulation of levator ani muscle.

[2] Estrogen therapy → post-menopausal atrophy.

- It causes thickening of the urethral mucosa and engorgement of the underlying blood vessels thus increasing the urethral pressure and resistance.
- It also stimulates the synthesis of collagen by the fibroblasts, and so increases the strength of pelvic connective tissue which supports the pelvic organs.
- Oestrogen is given orally or as vaginal cream.

[3] ↓ wt in obese patients.

[4] Hodge pessary to elevate and support the bladder neck.

[5] Stop caffeine and smoking.

[6] Alpha adrenergic stimulant.

[7] Injection of Teflon or bovine collagen → submucosal in bladder neck → narrowing of urethra → ↑ urethra resistance.

Surgical treatment: (It is the 1^{ry} treatment)

(1) Vaginal operations:

1. **Kelly operation:** plication of fascia around bladder neck.
2. **Kennedy operation:** plication of fascia all through length of urethra.
 - Both done in cases associated with prolapse.
 - Success rate is 55- 60%.

(2) Abdominal operations:

1. Marshall- Marrchetti- Krantz operation:

- Suture fascia around bladder neck and upper urethra to periosteum of pubic bone.
- Main complication is osteitis pubis.

2. Burch colposuspension:

- Suture fascia around bladder neck to iliopectineal ligament (Cooper's ligament) → It corrects stress incontinence and cystocele.
- Success rate of abdominal operation is 80- 90%.
 - Burch colposuspension is the operation of choice.
 - It can be done by laparoscopy.

(3) Combined abdominal and vaginal operations:

1. Sling operations:

- Sling is passed below the bladder neck and sutured the rectus sheath.
 - **Aldridge operation:** using rectus sheath.
 - **Pereyra:** nylon sling.

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2. Needle bladder neck suspension:

- Incision in ant. vaginal wall at level of bladder neck.
- Nylon sutures are passed from fascia around bladder neck behind symphysis pubis and attached to rectus sheath.
- Cystoscope may be used.
- Example: **Stamey operation** → use nylon, polyethylene.

Recent lines in treatment of stress incontinence:

(1) Tension- free vaginal tape: (TVT)

- Tape is made of prolene and has a curved needle at each end.
- Tape is passed below **mid-urethra**.
- Passed supra-pubic through the recti.
- Under cystoscopic guide to avoid puncture of bladder.

(2) Trans-obturator tape (TOT):

- Passed through obturator foramen.
- Support mid urethra.
- It avoids bladder perforation.
- * Success rate of TVT and TOT → 85%.

(3) Artificial bladder sphincter: When surgery fails to treatment SI.

Overactive bladder

Definition:

Overactive bladder is a problem with bladder storage function that causes a sudden urge to urinate. The urge may be difficult to suppress, and overactive bladder can lead to the involuntary loss of urine (incontinence).

Etiology:

The etiology of overactive bladder (OAB) is unclear, and indeed there may be multiple possible causes:

1. Local bladder irritation:

- Cystitis, stone, tumor.
- Many follow operations of SI.

2. Neurological disease: multiple sclerosis, parkinsonism, emotional instability.

- It is often associated with overactivity of the Detrusor muscle, a pattern of bladder muscle contraction observed during urodynamics.
- OAB is distinct from stress urinary incontinence, but when they occur together, the condition is usually known as mixed incontinence.

Symptoms:

- Strong, sudden urge to urinate.
- Urge incontinence, the involuntary loss of urine immediately following a desire to urinate.
- Frequency.
- Nocturia.

Investigations:

- The investigations are mainly aimed at ruling out other causes of overactivity of the bladder like infection, bladder tumor and calculus.
- Additionally, urine culture may be done to rule out infection.
- Cystourethroscopy may be done to exclude tumor and kidney stones.
- The diagnosis is confirmed by cystometry.

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Treatment:

1- Lifestyle modification (fluid restriction, avoidance of caffeine).

2- Bladder retraining (Bladder drills): The patient is instructed to pass urine every hour during day time and ↑ by ¼ h/ week till she can pass urine every 2-3 hours.

3- Medical:

- **Anticholinergics (antimuscarinic drugs):** Solifenacin, Oxybutynin, Tolterodine.
- **Tricyclic antidepressant:** imipramine hydrochloride (Tofranil), which also relaxes bladder muscles.
- **Botulinum toxin A (Botox):** injections into the bladder wall via cystoscope can suppress involuntary bladder contractions by blocking nerve signals and may be effective for up to 9 months.

4- Surgical (resistant cases):

- **Bladder augmentation:** uses part of the bowel to increase bladder capacity.
- **Detrusor myectomy.**

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Genito-urinary fistula

It is abnormal communication between genital tract and urinary tract.

Types:

[1] Ureteric:

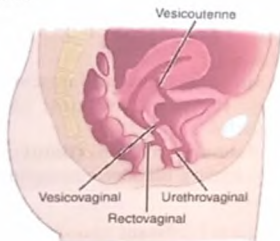
- Uretero-uterine.
- Uretero-cervical.
- Uretero-vaginal → 2nd commonest.

[2] Vesical:

- Vesico-uterine.
- Vesico-cervical.
- Vesico-vaginal → commonest.

[3] Urethral: - Urethro-vaginal.

Sometimes, more than 2 organs are involved: vesico-urethro-vaginal.



N.B.:

- Fistula is abnormal communication between 2 epithelial surfaces of hollow organs.
- Sinus: blind ended tract.

Vesico-vaginal fistula

Definition: It is abnormal communication between urinary bladder and vagina.

Incidence: The commonest type.

Causes:

[1] Congenital: It is very rare.

[2] Traumatic:

(A) Obstetric trauma: It is the commonest cause in the **Egypt and developing countries**.

Necrotic obstetric fistula:

- in case of obstructed labor, the bladder base and anterior vaginal wall are compressed for long period between pubic bone and fetal head → Ischemia of the compressed tissues → after 3-10 days.
- Also necrotic fistula may occur when the bladder is included during suturing the lower uterine segment in caesarean section.

Traumatic obstetric fistula:

- * Caesarean section.
- * Forceps delivery.
- * Bone speculles after craniotomy.
- * Incontinence develops immediately after delivery.

(B) Surgical trauma: The commonest cause in **developed countries**.

* **Abdominal operations:**

- Hysterectomy.
- Werthiem's operation.
- Repeated C.S.

* **Vaginal operations:**

- Vaginal hysterectomy.
- Anterior colporrhaphy.
- Mc-Indoe's operation.

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(C) Direct trauma:

- Falling on sharp object.
- Defloration injury.
- Fracture pelvis.
- Neglected pessary.

* Incontinence develops immediately after recovery from anesthesia in surgical and accidental trauma.

[3] Inflammatory:

- Pelvic abscess rupture in bladder and vagina.
- T.B.
- Bilharziasis.
- Syphilis.

[4] Neoplastic:

- Advanced cervical cancer.
- Vaginal cancer.
- Bladder cancer.

[5] Radiotherapy: Endarthritis obliteration and ischemic necrosis.

- * Fistula develops after several months or years.

Diagnosis:

(A) History:

- Differentiate between different types of incontinence.
- Determine the cause of fistula.
- Dating since birth → congenital fistula.
- Following labor:
 - o Immediately: traumatic obstetric fistula.
 - o After 1 week: necrotic obstetric fistula.
- Following gynecological operation → surgical fistula.
- History of pelvic infection → inflammatory fistula.
- History of pelvic malignancy → malignant fistula.
- History of pelvic radiotherapy → post-irradiation fistula.

(B) Symptoms:

• Incontinence of urine:

Type:

- o "True urinary incontinence" Complete: no urine is retained in bladder → no desire.
 - Low and large fistula.
 - D.D.: Bil. Ureteric fistula.
- o Partial: Some urine is retained in bladder → desire to micturate.
 - Small, high or valvular fistula.
 - D.D.: Unilateral uretrovaginal fistula.

Time of onset:

- o Immediate: direct obstetric trauma, surgical trauma.
- o After 1 wk: necrotic obstetric fistula.
- o After several months: post-irradiation fistula.
- Symptoms of 2^{ry} vulvitis:
Pain and soreness of the vulva due to continuous dribbling of urine.

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- Symptoms of urinary tract infection:
 - Suprapubic pain → cystitis.
 - Loin pain → pyelonephritis.
- Amenorrhea:
 - Psychological disturbance: commonest cause.
 - The cause of fistula is the cause of amenorrhea: hysterectomy.
 - Sheehan's syndrome.
 - Pregnancy (very rare with fistula).

(C) Signs:

- General examination:
 - Anemia.
 - Uremia.
- Abdominal examination:
 - Palpable kidney → hydronephrosis.
 - Tenderness of renal angle → pyelonephritis.
- Local examination:
 - Inspection:
 - Continuous leakage of urine.
 - Vulva: vulvitis + phosphatic incrustations (gritty sensation).
 - Vagina: inflamed + wet.
 - Palpation of anterior vaginal wall:
 - Speculum examination:

"By Sim's speculum in Sim's position → inspection of anterior vaginal wall".

- Value:

- 1- Detect site, size and number of fistula by inspection.
 - 2- Click test: metal catheter is passed through the urethra into bladder and uterine sound in the vagina → clicking sound.
 - 3- In small and high fistula → inject methylene blue into the bladders → methylene blue will pass through fistula into vagina.
- **Sim's position:** patient lies on her left side near the edge of the table with her left arm behind her back and right arm hold the edge of table, the right thigh and knee are fully flexed and left leg and thigh are extended → displaces intestine upward → -ve pressure in the pelvis → inflating vagina.
- Examination under anesthesia: help diagnosis.



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Investigations:

(1) Methylene blue test:

- The vagina is packed by 3 pieces of gauze.
- 200 cc of methylene blue is injected into the bladder by sterile rubber catheter which is then removed.
- The patient should walk for 10- 15 minutes.
- The lowest gauze is discarded.
- It differentiates between:
 - V.V. fistula. - Uretrovaginal fistula. - Stress incontinence.
- Result:
 - One or both pieces are stained blue → vesicovaginal fistula (high- low).
 - One or both pieces are soaked with urine → ureterovaginal fistula.
 - Both pieces are dry→other cause of incontinence (e.g. stress in continence).

(2) Cystoscopy: "in every case"

- Confirm diagnosis of V.V. fistula.
- Detect site, size and number of fistula.
- Determine relation of fistula to ureteric orifice.
- Detect associated pathology of bladder: cystitis, T.B.
- Exclude ureteric fistula:
 - No ureteric efflux on affected side.
 - If ureteric catheter is passed it will stop at site of lesion.
 - IV indigo carmine (4cc 4%) "chromocystoscopy" normally dye will appear from ureteric orifice after 4 minutes.
- In case of v.v. fistula near ureteric orifice: a ureteric catheter is passed pre-operative to facilitate palpation of ureter during surgery.

How to do cystoscopy in cases with V.V. fistula ?

- To allow filling of bladder with fluid → put a finger or pack on vagina.
- Or introduce cystoscope with patient in knee chest position to create -ve pressure → allows distension of bladder "indirect air cystoscopy".
- Or male condom is fixed to tip of cystoscope and distended with fluid after cystoscope is introduced into bladder.

(3) IVP "Intra venous pycelography":

- Assess kidney function.
- Diagnose hydroureter and hydronephrosis.
- Exclude ureteric fistula.
- Delineate course of ureter.

(4) Urine analysis and culture and sensitivity : Urine is collected by a catheter or a piece of cotton in the vagina.

(5) Kidney function test: Urea, creatinin and electrolytes.

(6) Routine pre-operative investigations: CBC, ECG.

Management:

Prophylaxis:

- Bladder should be kept empty in the following:
 - Before labor.
 - Before operation: C.S. and hysterectomy.
- Early detection and management of obstructed labor.

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- Careful obstetric maneuvers.
- Proper mobilization of bladder during C.S and hysterectomy.
- Bladder injury discovered during surgery → immediate repair + catheter for 10- 14 days.
- Invasive carcinoma of cervix (early detection- proper management).
- After successful repair of V.V. fistula → delivery by C.S.

Active treatment:

- In case of inflammatory or malignant fistula, the treatment is that of the primary cause.
- In case of congenital or traumatic fistula, the treatment is surgical repair.

(A) Timing of operation:

- Fistula discovered after labor or operation → fix Foley's catheter for 10- 15 days + antibiotics → fistula may heal completely or become smaller.
- Repair after 3-6 months after injury or previous repair.
- Post-menstrual → ↓ blood loss due to pelvic congestion.

(B) Pre-operative preparation:

- Pre-operative investigations.
- Treatment of the following:
 - Anemia.
 - UTI.
 - Vulvitis: vasline or zinc oxide.
 - Phosphatic incrustations: scrapping and resulting ulcers are painted with silver nitrate.
- Oestrogen locally or by mouth for atrophic tissues in postmenopausal patients.

(C) Operations: for details refer to operative gynecology section

1) Vaginal repair:

[1] Dedoublement "flap splitting operation":

- The vagina is separated from the bladder and each organ is closed separately.

[2] Saucerization "Sim's operation":

- An elliptical incision is made in the anterior vaginal wall.
- The fistula is excised removing wider part from the vagina than the bladder avoiding bladder mucosa.
- The edges of the bladder and vagina are sutured together.
- Done in case of: High inaccessible fistula surrounded by dense scar tissue.

[3] Latzko operation:

- It is preferred in post-hysterectomy vault fistula.
- The upper part of vagina is removed. The hole in bladder is closed and followed by closure of vagina.

[4] Post-irradiation fistula:

- The blood supply to region is impaired due to endarteritis. A flap using bulbocavernosus muscle is used → Martius graft.

2) Abdominal repair:

Indications:

- Failure of vaginal repair.
- High inaccessible fistula vaginally.
- Narrow vagina due to excessive fibrosis.

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Types:

- Intra peritoneal: transvesical-extravesical.
- Extra peritoneal: transvesical-extravesical.
- The transperitoneal approach is used when the extraperitoneal approach is difficult or an omental graft is indicated.

(D) Post-operative care:

- **Catheter care:** observation/2h → amount, colour and reaction of urine:
 - If no urine passes through catheter for 2 hours:
 - Blockage of catheter (blood clot/phosphate deposits): treatment by gentle injection of saline or catheter is replaced.
 - Anuria.
 - Bloody urine:
 - Bladder wash by silver nitrate 1%.
 - If excessive bleeding → exploration.
 - Alkaline urine: bladder wash by ammonium chloride.
 - Removal of catheter **after 14 days**.
- **Vaginal pack:** removed after 24h.
- **Antibiotics:** to prevent infection.
- **Fluids:** large quantities 3L day.

Subsequent management:

- After removal of catheter: the patient should micturate every 2h by day and 4h by night → avoid distension.
- She must remain under observation for one month.
- Sexual intercourse: avoided for 3 months.
- Pregnancy: no pregnancy for 1y.
- Delivery: C.S. "upper segment".

(E) Complications:

(1) Operative:

- Anesthetic complications.
- Shock. - 1ry hemorrhage.
- Injury: ureter- bladder.

(2) Post-operative:

- **Early:**
 - Pulmonary complication (DVT → embolism).
 - Hemorrhage "reactionary or 2ry".
 - Infection "wound and UTI".
- **Late:**
 - Recurrent fistula.

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Recurrent vesico-vaginal fistula

Definition:

Recurrence after 6 months following successful repair.

Causes:

(A) Preoperative

- Bad general condition:
 - Anemia- uremia
- Bad preparation:
- UTI- Vaginitis.
- Bad time of operations
 - Premenstrual.
 - Immediate:
 - Post partum.
 - Post operative.

(B) Operative

- Failure to recognize other fistula.
- Bad choice of operation.
- Poor surgical technique.
 - Poor hemostasis.
 - Sutures were under tension
 - Eversion of the mucosa or the presence of suture material on the vesical side favour deposition of phosphate crystals.

(C) Post-operative

- Urinary bladder distension (obstruction of catheter).
- Infection.
- Haematoma.
- Early intercourse < 3m.
- Early pregnancy < 1 year.
- Bad management of labor.

Treatment:

After 3-6 months

The choice of operation depends on several factors including the size and site of fistula, the extent of scarring, the number of previous operation, and the age of the patient. The alternative lines of treatment are:

- Vaginal repair may be tried at first.
- Abdominal repair is tried after failure of vaginal.
- Repeated failure to repair fistula:
 - Colpocleisis.
 - Ilial conduit.
 - Urine diversion: uretero-colic implantation (malignant fistula).

NB: Combined vesicovaginal and rectovaginal fistulae: Both can be repaired in one sitting, but there is no golden rule which one is closed first. Also, one fistula may be closed first and the other one later on.

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Uretero-Vaginal Fistula

Etiology:

- Congenital: very rare.
- Traumatic:
 - Surgical trauma:
 - * Dangerous sites → see before.
 - * Operations → see before.
 - * Type of injury → see before.
 - Obstetric trauma: very rare (rupture uterus).
 - Direct trauma: fracture pelvis- vaginal rupture.
- Post-irradiation: very rare.

Diagnosis:

History: Like V.V. fistula.

Symptoms:

- Incontinence of urine: (true)
 - Usually partial "unilateral ureteric fistula".
 - May be complete "Bilateral ureteric fistula or unilateral fistula and other kidney is non functioning".
- Vulvitis and vaginitis.
- Urinary tract infection.
- Psychological disturbance.

Signs:

- General: As V.V. fistula.
- Abdominal: As V.V. fistula.
- Local: site of fistula: usually in lateral vaginal fornix.
- Examination under anesthesia.

Investigations:

- **Methylene blue test:** the upper piece of gauze is soaked with urine.
- **Cystoscopy:** - Intact bladder +
 - No ureteric efflux on affected side.
 - If ureteric catheter is passed → it will stop at site of fistula.
 - Chromocystoscopy "4cc IV indigocarmine 4% will appear after 4 minutes".
- **IVP:**
 - The course of the ureter is interrupted at site of the fistula and lower end may not be seen.
 - Diagnose hydronephrosis.
 - Assess kidney function.
- **Urine analysis.**
- **Kidney function.**
- **Routine pre-operative investigation.**

Management:

Prevention:

- How to protect the ureter ?
- If injured during surgery → immediate repair.

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Active treatment: Abdominal operation:

- Re implantation of ureter in the bladder.
- Rolled bladder flap "Boari's flap".
- End to end anastomosis.
- Transverse ureteric implantation.
- Ilial conduit.
- Ureterocolic implantation.

Post-operative care:

- Ureteric stent → 1 month "removed by cystoscope".
- Antibiotics.
- Fluids.
- Pregnancy and labor "C.S."

Complications of urinary fistulas:

- Urinary tract infection, stone formation and renal failure.
- Hydroureter and hydronephrosis due to ureteric stenosis caused by fibrosis at the site of the ureteric fistula.
- Vulvitis, vaginitis and formation of Phosphatic deposits on the vulva.
- Vaginal stenosis due to scarring. Stones may form in the vagina.
- Psychological disturbances as amenorrhoea.

Menouria syndrome (Vesico-uterine fistula)

- The patient complains of cyclic hematuria during menstruation.
- Cause: vesico-uterine fistula by lower segment C.S.
- Diagnosis:
 - Cystoscopy
 - Hystero-graphy
 - Hysteroscopy
- It is called Yousef syndrome (1957).
- Treatment: Abdominal repair.

Urethero-vaginal fistula

- Usually traumatic.
- No incontinence "injury below sphincter".
- During micturition:
 - Double stream.
 - Urine dribbles from the vagina.
- Treatment: Vaginal repair.

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Old complete perineal tear

Definition:

A perineal tear with injury of external anal sphincter with or without injury of rectum and anal canal which is not sutured immediately.

Characters:

- Complete perineal tear not sutured immediately or breakdown of sutured perineal tear.
- Heal by granulation tissue: external anal sphincter does not heal properly → weak. Vaginal introitus → wide and lax.
- It may cause:
 - Prolapse: rare ?? But common with 2nd degree.
- Sexual dysfunction.

Degrees of perineal tears:

Incomplete:

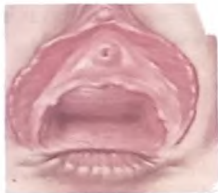
- 1st degree: tear of vaginal mucosa and perineal skin.
- 2nd degree: all the above + perineal muscles except external anal sphincter.

Complete:

- 3rd degree: all the above + external anal sphincter.
- 4th degree: all the above + rectal or anal mucosa.

Etiology:

- Obstetric trauma:
 1. Over stretch of perineum "macrosomia".
 2. Rapid stretch of perineum: precipitate labor.
 3. Inelastic perineum: scarring, edema, rigidity.
- Accidental trauma:
 1. Falling on sharp object.
 2. Car accident.
 3. Defloration injury.



Clinical picture:

(1) Symptoms:

- Involuntary passage of flatus and fluid stool (patient controls hard stool by contraction of levator ani).
- Soreness of vagina due to irritation by faeces and 2ry vulvities.
- Sexual dissatisfaction.
- Vaginal flatus (garrulitas vulvae).

(2) Signs:

- Tear is seen in the perineum extending to anal opening.
- Short perineum and anal orifice is almost in contact with introitus.
- Dimple on each side of anus indicating retracted torn ends of external anal sphincter.
- Absence of corrugation around the anus except posteriorly.
- Absence of sphincteric control (Index finger test): index finger is introduced easily in anus without resistance.
- If rectal wall is torn: rectal mucosa appears bright red in the lower part of defect.

Management:

Prophylaxis:

- Proper management of labor.
- Episiotomy when indicated.
- Immediate repair of perineal tears.

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Active treatment:

[1] Pre-operative preparation:

1. Timing: 3- 6 month after labor:

- To allow healing of granulation tissue.
- Absorption of scar tissue.
- Tissues become strong enough to carry sutures.

2. Patient is admitted to hospital 3 days before surgery:

- Low residue diet (avoid milk) → fluids for 72 hours.
- Treatment of any genital infections.
- Intestinal antiseptic: neomycin (1000 mg/6h) + metronidazol (500 ml/t.d.s)
- Daily vaginal douch and saline enema 2 times daily.
- The day before operation: 20 ml of manitol each hour for 6 hours is given orally.

[2] Operations:

1. Standard repair:

- H-shaped incision is done:
 - Horizontal limb at mucocutaneous junction.
 - Vertical limbs at site of dimple.
- Incision is deepened to expose different structures of perineal body.
- Vagina is separated from rectum, ends of external anal sphincter are identified.
- Suture rectal and anal wall by interrupted inverting Lambert sutures (2 layers).
- Suture torn ends of external anal sphincter.
- Suture the levator ani muscle.
- closure of vaginal mucousa.
- Suture superficial and deep perineal muscles by interrupted sutures.
- Close of skin.

2. Warren's flap operation:

- Indicated in (great loss of tissue - recurrence after standard repair).
- V-shaped flap from vaginal mucosa is turned down to close defect in rectal mucosa.

3. Rectal advancement: "Nobel- Mengert operation"

→ Indicated in case of large defect.

[3] Post-operative care:

1. Vulva and perineal wound:

Are kept dry and clean. After each micturition or defecation → perineum is washed by antiseptic solution, dried, sprayed with antibiotic → sterile vulval pad.

2. Systemic antibiotic (cephalosporin's: 500mg/6h) + intestinal antiseptics (7 days).

3. Feeding:

- Nothing per mouth for 48h → only IV fluids.
- Low-residue diet (fluids- avoid milk) → for 48h.
- Soft diet for 24h.

4. On fifth day → castor oil purge (60 ml) then the patient is given liquid paraffin for 2 weeks.

5. No sexual intercourse for 3 months.

6. Subsequent deliveries: Medio-lateral episiotomy or by C.S.

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Recto-vaginal fistula

Etiology:

(1) Congenital: rare.

(2) Traumatic:

A) Obstetric trauma:

- Incomplete healing of 4th degree perineal tear or inclusion of rectum in stitch during repair episiotomy "The commonest".
- Necrotic obstetric fistula: obstructed labor → ischemia necrosis of rectovaginal septum.
- Traumatic obstetric fistula: bony specules- instruments.

B) Surgical trauma: Injury of rectum during:

- Posterior colpoproctopexy.
- Hysterectomy.

C) Accidental trauma:

- Falling on sharp object → stab wound.
- Defloration injury.
- Ulceration of neglected pessary or F.B.

(3) Inflammatory:

- Pelvic abscess opens into rectum and vagina.
- Syphilis, tuberculosis, Bilharziasis of rectum or vagina.

(4) Neoplastic: advanced rectal, vaginal, cervical carcinoma.

(5) Post-irradiation fistula: endarteritis obliterans → ischemia and necrosis.

Diagnosis:

(1) Symptoms:

- Large fistula: loss of voluntary control over stool and flatus.
- Small fistula: loss of voluntary control of liquid stool and flatus.
- Vaginal discharge (2ry vaginitis).

(2) Signs:

- Exposure of posterior vaginal wall with good light.
- Small fistula is diagnosed by rectal- rectovaginal examination.
- Small probe is passed in fistulous tract → palpated by P/R.
- Methylene blue injected into rectum.

Treatment:

[1] Prophylaxis:

- Proper repair of perineal tear and episiotomy.
- Proper management of labor (obstructed L.).
- Careful instrumentation.

[2] Active treatment:

(A) Pre-operative: As old complete perineal tear.

(B) Operations:

1. Inflammatory and malignant → treatment of cause.
2. Congenital and traumatic → surgical repair.

1) Fistula of lower 1/3:

Lawson-Talt:

- Done in case of large fistula and perineal body below fistula is inadequate.
- Convert fistula into complete perineal tear then repaired.



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Vernon- David:

- Done in case of small fistula and perineal body is intact.
- Circular incision is made in vagina around fistula.
- The fistula is then dissected and inverted into rectum → to undergo sloughing.
- The opening in rectal wall is closed.
- Levator ani muscles are approximates.
- The vagina is closed.

2) Fistula in middle 1/3: flape-splitting operation (As v.v. fistula).

3) Fistula of upper 1/3: Abdominal repair.

- In cases of very large fistula → temporary colostomy.
- 2 week before repair.
- closed after healing of fistula (>6w).

4) Malignant fistula:

- Temporary colostomy.
- Treatment of malignancy.

(C) Post-operative care:

Like old complete perineal tear.

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Gynecologic Oncology

Cervical Intra Epithelial Neoplasia (CIN)

Definitions:

Cervical intra epithelial Neoplasia (CIN): Malignant change involving different levels of epithelial lining of cervix with no invasion of basement membrane. It includes dysplasia & carcinoma in situ.

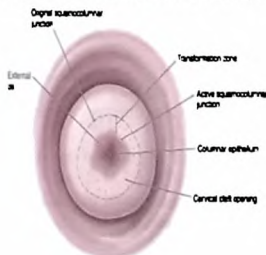
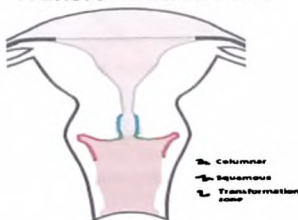
Cervical Dysplasia: squamous basal cell hyperplasia, neoplastic atypia & disordered stratification which is partly preserved.

Carcinoma in situ (CIS): whole thickness of stratified squamous epithelium is replaced by atypical cells with no invasion of B.M.

Pathogenesis:

- **Transformation zone (TZ):** is the area between the original squamo-columnar junction (SCJ) (below) and the new SCJ (up).
 - The original squamo-columnar junction (SCJ) (below): junction between squamous epithelium covering ectocervix & columnar epithelium of endocervix.
 - The new SCJ (up): junction formed later on in life due to change of columnar to squamous epithelium near puberty.
- The transformation zone is the most susceptible area for CIN & cancer to arise.
- In the transformation zone, *squamous metaplasia* occurs where columnar epithelium is changed to squamous epithelium. This is called *physiological metaplasia* and is more active at puberty & age of 1st pregnancy.
- In the presence of the risk factors and in particular if there is reduced host immunity, *pathological metaplasia* occurs.
- In case of pathological metaplasia, the columnar cells change to dysplastic cells (CIN). This can further progress to cancer or regress to normal.
- **In summary:** In presence of HPV infections (type 16 & 18), progression to CIN & cancer or regression to normal depends on several factors that interfere with host ability to clear the virus

Transformation zone



Incidence: CIN is more common in:

- **Age:** Average age is 35 years.
- **Race:** Black.
- **Parity:** High parity.
- **Socioeconomic level:** Low Socioeconomic levels.

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Risk Factors for Cervical Neoplasia:

1- Sexual activity:

Sexually active woman are 2-4 times more likely to develop cancer cervix than non sexually active woman specially:

- o Early age of coitus <20 years.
- o Increase number of partners "common in prostitutes and rare in nuns".
- o Male promiscuity.

❖ Relationship between sexual activity and cervical carcinoma:

- o Cervical epithelial cells phagocytose spermatozoa which provide cells with large quantities of nucleic acid which stimulate abnormal epithelial activity. This is more in replacement epithelium than in mature tissues.
- o Sexual activity is associated with increased incidence of STD e.g. HPV.

2- Sexually transmitted diseases (STD):

o Human papilloma virus (HPV):

- It was proved on molecular basis to be a risk factor for cervix.
- DNA of virus is integrated on host cell DNA: carcinogenesis.
- High risk types "16-18".
- Moderate risk types "31, 33, 45 etc.)".

o Herpes simplex virus "HSV":

- It was not proved on molecular basis but it is possible association.

3- Immunodeficiency:

- Patients with AIDS and organ transplantation are more liable to develop cancer

4- Smoking:

- Products of smoking are concentrated in cervical mucous and may produce changes in DNA of cells.
- Smoking increases squamous cell carcinoma.

5- Combined pills:

- May increase adenocarcinoma.

6- Repeated cervical trauma and chronic infection.

Pathology:

Macroscopic appearance:

- Usually, no lesion is seen by Naked eye.
- The cervix looks normal or may show an associated non-specific lesion as erosion (ectopy). Cervicitis or leukoplakia (suspicious cervix).

Microscopic appearance:

- The presence of abnormal immature basal cells above the lower most layers in the epithelium indicates (dysplasia).
- As the hyperplastic abnormal cells extend from the basal layer onwards towards the surface the severity of the lesion increases.

Criteria of dysplasia:

- Large cells with increased nuclear cytoplasmic ratio,
- Pleomorphism,
- Hyperchromatosis,
- Abnormal mitosis,
- Multiple nucleoli and
- Loss of stratification.

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Classification:

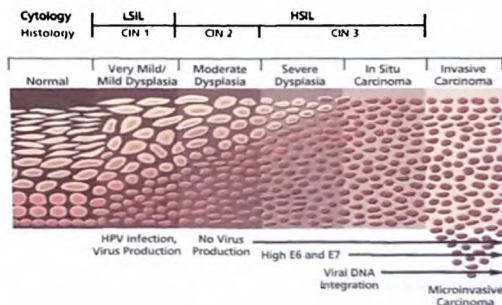
1) Conventional histologic classification:

- CIN I: "mild dysplasia": abnormal cells in lower 1/3 of epithelial thickness.
- CIN II: "moderate dysplasia": abnormal cells in lower 2/3 of epithelial thickness.
- CIN III: "severe dysplasia": abnormal cells > 2/3 of epithelial thickness but there are some mature cells on surface.
- Carcinoma insitu: whole thickness of epithelium is replaced by abnormal cells but with no invasion of B.M.

2) The 2001 Bethesda system:

o Squamous Cell:

- Atypical squamous cells
 - of undetermined significance (ASC-US)
 - cannot exclude HSIL (ASC-H)
- Low grade squamous intraepithelial lesion (LSIL): encompassing: HPV/mild dysplasia/CIN 1
- High grade squamous intraepithelial lesion (HSIL) encompassing: moderate and severe dysplasia, CIS/CIN 2 and CIN 3
- Squamous cell carcinoma
- o Atypical glandular cells (AGC):
 - Not otherwise specified (AGC-NOS)
 - Favor neoplasia (AGC-favor neoplasia)
 - Adenocarcinoma in situ (AIS).
 - Adenocarcinoma.



Diagnosis:

- There is neither symptoms nor signs for CIN, so diagnosis can be established only by screening.
- Rarely: predisposing factor "HPV" or association with chrorionic cervicitis, cervical erosion, leukoplakia (Suspicious cervix).

Course and fate:

- Regresses.
- Persists and remains unchanged.
- Progresses to invasive cancer (CIN I 15%, CIN II 25%, CIN III 50%).

Investigations "Screening for cancer cervix":

- Cytology "cervico-vaginal smear".
- Colposcopy.

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- Schiller's iodine test.
- Biopsy.
- 1) Cytological study "cervical smear" pap smear:
 - Idea: study morphological changes in exfoliated cell.
 - Precautions:
 - No douching or intercourse for 2 days.
 - No p/v or use of lubricant.
 - Technique:
 - A- Sampling:
 - Vaginal smear: Aspiration of fluid from posterior vaginal fornix by pipette or the vaginal end of spatula.
 - Cervical smear: Obtained by scraping T.Z by cervical end of spatula "Wooden Ayre's spatula"
 - 3- Endocervical swab by cotton tipped swab or cytobrush.
 - B- The drop is spread over a slide.
 - Fixed on alcohol 95% or better immerse the slide into special liquid (Liquid based cytology).
 - Stained with papanicolaou stain then examined microscopically.
 - Interpretation:
 - Negative: no malignant cells.
 - Suspicious: (doubtful): Negative but containing atypical cells suspicious of malignancy
 - Positive "Grossly malignant cells"
 - Advantages:
 - Easy.
 - Early diagnosis.
 - Office procedure
 - Accurate (98%).
 - Disadvantages:
 - False positive:
 - Some infections may mimic picture of CIN (HPV).
 - Atrophic post-menopausal (No proper maturation).
 - False negative:
 - Tumors not shedding cells "infiltrative and endocervical".
 - Bad technique or cytologist.
- However: proper examination and use of DNA analysis → decrease false positive or false negative.
 - It requires expert cytologist.
- 2) Colposcopy:
 - It is done in cases with positive smear to select site of biopsy.
 - Magnifies Cervix. 10-40 times.
 - Normal findings:
 - Normal squamous epithelium: smooth, pink and glistening.
 - Normal columnar epithelium: polypoidal, red and translucent.
 - T.Z: is junction between squamous epithelium and columnar epithelium with glandular opening.
 - Abnormal findings:
 - Leukoplakia: white epithelium before application of acetic acid.
 - Aceto-white area: white epithelium after application of acetic acid.



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- Abnormal vascular pattern: "By green filter"
 - Punctuation: stippling capillaries.
 - Mosaic pattern.
 - Coma shaped, spaghetti shaped and cork screw.

N.B.: Cervicography: Special camera used to photograph cervix after application of acetic acid and film is sent and examined by expert.



3) Schiller's iodine test:

▪ Indication:

Positive smear and coloscope is not available to select site of biopsy.

▪ Technique:

Cervix. is painted by Lugol's iodine 0.3% or Schiller's iodine (1-part iodine + 2 part KI + 300-part water).

▪ Result:

- Healthy squamous epithelium: contain glycogen: stains brown.
- Abnormal epithelium "Ulcers, erosion and malignancy": no glycogen and the site of biopsy doesn't take the stain

4) Cervical biopsy:

It must be done to confirm diagnosis of CIN and exclude invasive carcinoma.

▪ Types of biopsy:

(1) Punch biopsy:

- Single or multiple from all suspected areas by colposcopy or schiller's iodine.

(2) Cone biopsy:

- Cone is removed using scalpel or diathermy or laser.
- Apex of the cone is close to internal os.
- Base of the cone circumcising the external os. Including all abnormal areas on portio-vaginalis.

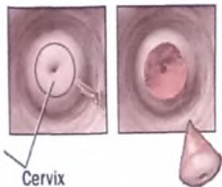
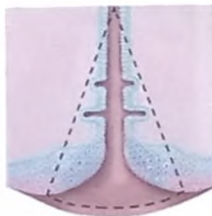
▪ Indication of conization:

A- Diagnostic:

- o Abnormal cytology and normal colposcopy.
- o Abnormal cytology and colposcopy not available.
- o Upper end of the lesion can not be visualized by colposcopy.
- o Whole TZ can not be visualized by colposcopy.
- o Suspected microinvasion.

B- Therapeutic:

- o CIN III, CIN II in young patient.
- o Endocervical lesion.
- o Cancer cervix stage Ia1 (fertility sparing).



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- **Complication of conization:**
 - Primary or 2ry hemorrhage.
 - Infection.
 - Incomplete excision.
 - Cervical stenosis: dysmenorrhea, haematometra, infertility and cervical dystocia.
 - Incompetent cervix: habitual abortion, preterm labor.
- **Contraindication of conization:**
 - Macroinvasive lesion.
 - Pregnancy.
- **Other types of cervical biopsy:**
 - Wedge biopsy.
 - Ring biopsy.
 - Four quadrant biopsy.

Treatment:

CIN I:

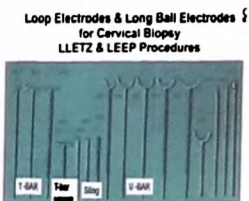
- 1- Treatment of inflammatory conditions.
- 2- Cytological follow up

CIN II:

(A) Ectocervical lesion:

1) Ablation and follow up by cytology.

Principle: Destruction of the lesion and the transformation zone with a safety margin of 5-10 mm around and in the depth.



Forms of ablation:

- Cryocautery.
- Electrocautery.
- Laser vaporization (CO₂).
- Diathermy cautery.

2) Excision of the lesion and the whole transformation zone is carried out by laser or by a diathermy loop

- 1- Large loop excision of the transformation zone: LLETZ
- 2- Loop electro surgical excision procedure LEEP.

Follow-up: by cytology.

(B) Endocervical lesion:

Conization and follow up by cytology.

CIN III:

- 1- Young patient: Like CIN II.
- 2- Old patient: Total hysterectomy with removal of a cuff from upper vagina.

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- **Indication of hysterectomy in treatment of CIN:**
 - Women above 40 years.
 - Patients requesting sterilization.
 - Associated pathology e.g. fibroid, adenomyosis.
 - Difficult to follow up by cytology or Colposcopy
- **Follow up by cytology:**
 - Every 3 months —» 1 year.
 - Then every 6 months —» 5 years
 - Then yearly indefinitely.

Invasive cervical carcinoma

Definition:

It is malignant change of epithelial lining of cervix with invasion of B.M.

Epidemiology:

- 2nd commonest cancer in women worldwide (after endometrial cancer).
- Most common cause of death from cancer in women.
- The incidence is reducing because of the comprehensive cytological screening programme which allows early diagnosis and treatment of the pre malignant lesions (CIN).

Age:

Two peaks of age: 30-40 years and Early 80s.

Risk factors:

Mentioned detailed in CIN

- 1) Early intercourse.
- 2) Early age at 1st pregnancy.
- 3) High number of sexual partners.
- 4) High parity (rare in nuns).
- 5) Low socioeconomic status.
- 6) Low immunity.
- 7) Smoking.
- 8) Human papilloma virus (HPV) infection (16, 18, 45, 31, 33). HPV infection is present in 99.7% of cases of cancer cervix is

Pathology:

1- Ectocervical carcinoma (carcinoma of portio-vaginalis): 85 %

It arises from squamous epithelium of the portio-vaginalis and always starts in the transformation zone.

Macroscopic picture:

- 1) **Hypertrophic "exophytic type":**
 - It is the commonest type
 - Cauliflower like mass: fungating, friable, necrotic and highly vascular.
- 2) **Ulcerative "endophytic type":**
 - Raised everted edge, friable necrotic floor and indurated base.
- 3) **Infiltrative "nodular type":**
 - Flate indurated nodule may ulcerate later.

Microscopic picture:

1- Squamous cell carcinoma 90%

2- Rarely adenocarcinoma: on top of columnar epithelium of cervical erosion.

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2- Endocervical carcinoma (15%):

It arises from columnar epithelium lining endocervical canal.

Macroscopic:

- It gives rise to ulcerative or diffuse infiltration type.
- Cervix is hard indurated barrel shaped.

Microscopic picture:

- Adenocarcinoma 50%
- Squamous cell carcinoma 50%: on top of squamous metaplasia

Histological grading:

1- WHO classification:

| | LARGE CELL KERATINIZED | LARGE CELL NON-KERATINIZED | SMALL CELL NON-KERATINIZED |
|----------------|---------------------------|----------------------------|----------------------------|
| Incidence | 15 -20 % | 70 -75 % | 5 % |
| Site of origin | Portiovaginalis | T.Z. | Endocervix |
| Cells | Large cells + keratin | Large cells + no keratin | Small cells + No keratin |
| Pattern | Nests + epithelial pearls | Nests + No pearls | Sheets of malignant cells |
| Prognosis | Intermediate | The best | The worst |

2- Broader's classification:

- Grade 1: Nests > 75 % (0 -25% are undifferentiated).
- Grade 2: Nests 50: 70% (25-50% are undifferentiated).
- Grade 3: Nests 25: 50% (50-75% are undifferentiated).
- Grade 4: Nests < 25% (75-100% are undifferentiated).

Spread:

Direct spread:

- **Forward:** to the bladder.
- **Backward:** rectum and uterosacral ligament.
- **Downwards:** vagina.
- **Upward:** uterus.
- **Laterally:** parametrium causing compression of ureter rather than infiltration leading to hydronephrosis and hydroureter and **Uremia** which is the commonest cause of death.

Lymphatic spread: By permeation and embolization.

Primary relay:

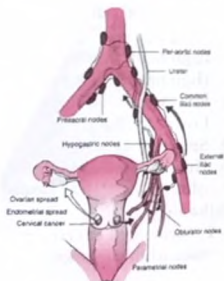
- o Paracervical and ureteric L.N "at crossing of uterine artery over ureter.

Intermediate relay:

- o Obturator L.N.: must be removed in every case.

External iliac L.N.:

- Medial group: medial to vein "most important"
- Anterior group: between artery and vein.
- Lateral group: lateral to artery.
- o Internal iliac L.N.: called hypogastric group.



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Deep relay:

- - Common iliac and paraaortic L.N.
- - Sacral "pre-sacral, lateral sacral" then paraaortic L.N.

Blood spread:

To distant organs Blood, Brain, Liver and Lung.

Direct (surface) implantation: Very rare, it occurs during operation.

Staging (clinical staging):

- EUA: (including rectovaginal examination) to assess the size of tumour, parametrium spread and extension to rectum and rectovaginal septum.
- Cystoscopy and Sigmoidoscopy to assess bladder and bowel involvement.
- Biopsy of suspicious areas.
- Chest X-ray.
- CT and MRI for further information about tumour size, nodal involvement.

"FIGO 2009" classification:

- **Stage I:** Invasive carcinoma limited to Cervix. or extend to body of uterus.

IA: Microinvasive carcinoma "diagnosed by microscope"

IA1: stromal invasion below B.M ≤ 3 mm in depth and ≤ 7 mm in width.

IA2: stromal invasion below B.M $3-5$ mm in depth and ≤ 7 mm in width.

IB: Clinically visible lesion limited to Cervix or microscopic lesion $> IA2$.

IB1: visible lesion ≤ 4 cm in greatest diameter.

IB2: visible lesion > 4 cm in greatest diameter.

- **Stage II:**

IIA: Involvement of upper $2/3$ of vagina.

IA1: lesion ≤ 4 cm in greatest diameter.

IA2: lesion > 4 cm in greatest diameter.

IIB: Infiltration of parametrium on one or both sides but not reaching lateral pelvic wall.

- **Stage III:**

IIIA: Involvement of lower $1/3$ of vagina.

IIIB: Infiltration of parametrium up to lateral pelvic wall or cases with hydronephrosis or non-functioning kidney due to the mass.

- **Stage IV:**

IVA: Spread to bladder or rectal mucosa.

IVB: Spread outside pelvis "distant spread".

NB: Bullous edema of bladder doesn't indicate involvement of bladder mucosa.

Diagnosis:

Symptoms:

Early cases are asymptomatic.

Vaginal bleeding: (the earliest symptom)

Early: Contact bleeding after coitus, douching and P/V.

Late: Continuous and massive bleeding.

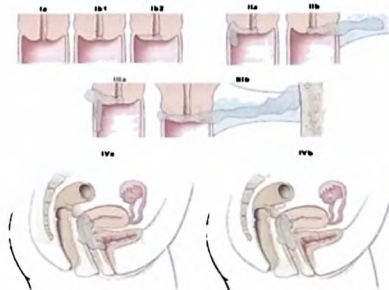
3- Vaginal discharge: 1st watery or mucoid then purulent offensive then blood stained.

4- Pain: Late symptoms due to spread out side cervix.

- Bladder: frequency, haematuria. - Ureter: ureteric colic.

- Rectum: tenesmus. - Pyometra: supra-pubic pain.

- Parametrium: deep seated pain.



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5- Symptoms of complication: cachexia, uremia, haemoptysis.

Signs:

i. General examination:

Cachexia, evidence of uremia, left supraclavicular or inguinal lymph nodes metastases, and edema of lower limbs metastasis.

ii. Abdominal examination:

Enlarged liver, kidneys, abdominal masses, and ascites.

iii. Pelvic examination:

Vaginal: Malignant mass is characterized by indurated base, friability on surface, contact bleeding, necrosis and infection.

Bimanual examination:

- Mobility of cervix.
- Involvement of parametrium "induration of parametrium" due to spread of malignancy and infection.
- Associated uterine or ovarian pathology.

Speculum examination:

- Cauliflower mass, ulcer, nodule and Barrel shaped cervix "endocervical carcinoma".
- Uterine sound: friability and bleeding "Clark's sign"

P/R: To examine: parametrium, uterosacral ligament and rectal mucosa.

Investigations:

Cervical biopsy:

- It must be done in every case to confirm the diagnosis and to classify the tumour according to its degree of malignancy.
- A punch or a wedge biopsy is taken and it is preferable to include an area of healthy tissue for comparison.
- Fractional curettage is done if suspect endocervical carcinoma.

Examination under general anaesthesia:

Must be done to determine extent of the growth. It is essential for clinical staging.

Imaging:

- **Computerized tomography (CT)** scans to the pelvis and abdomen. It shows the size of the tumour, infiltration of the parametrium, metastases in the pelvic and aortic lymph nodes and liver, and diagnoses hydronephrosis. It cannot differentiate between malignant and inflammatory nodes.
- **Magnetic resonance imaging (MRI)** is more accurate than CT scan.
- **Intravenous pyelogram** to show the condition of the ureters and kidney function. Must be done to diagnose the stage of the disease (hydronephrosis or nonfunctioning kidney indicates stage III).
- **Chest x-ray.**

Preoperative preparation:

CBC, RBS, Urine analysis, Kidney function test, liver function test, ECG

Others:

- Cystoscopy: infiltration of bladder.
- Proctoscopy: infiltration of rectum.

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Differential diagnosis:

A. Ulcerative lesions:

- Cervical erosion: bright red, no friability or induration and biopsy.
- T.B ulcer: serpiginous outline, undermined edge, yellow floor, no induration or friability.
- Bilharzial ulcer: history, greyish floor, ova is detected in scraping.
- Chancre: round, punched out edge, spirochetes are detected.
- Trophic ulcer of prolapse: no induration, friability or necrosis.
- Infected traumatic lesion: cervical laceration.
- Herpetic ulcer: shallow, multiple, small ulcer.

B. Polypoidal lesion:

- Adenomatous (mucous) polyp.
- Fibroid polyp.
- Bilharzial polyp.
- Tuberculous polyp.
- Condylomata accuminata.

C. Endocervical carcinoma "causes of barrel shaped cervix":

- Chronic hypertrophic cervicitis.
- Interstitial cervical fibroid.
- Retained products of conception (cervical abortion).
- Cervical ectopic pregnancy.

Complication:

I – General complications of malignancy:

- Cachexia.
- Distant spread.
- Infection.
- Hemorrhage.
- Complication of treatment.

II – Specific complications:

- Uremia: is commonest cause of death due to ureteric obstruction and UTI.
- Malignant fistula.
- Obstruction of cervical canal: haematometra, pyometra.

Causes of death in order:

- Uremia: is the commonest cause of death.
- Hemorrhage 2nd cause.
- Intercurrent infection: parametritis, peritonitis and cachexia.
- Complication of distant spread.
- Pulmonary embolism.
- Complication of therapy.

Treatment:

I- Prevention:

- Human papilloma virus vaccines:

- Gardasil® quadrivalent vaccine against types: 6, 11, 16, and 18 or Cervarix® bivalent vaccine against HPV types: 16 and 18.
- Both given as three intramuscular injections over a 6-month period.

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- Both can be given routinely at ages 11 or 12. Vaccination is also recommended for girls and women ages 13 to 26 who have not been vaccinated already or who did not complete the three-dose series.

- Avoid multiple partners, early marriage.
- Screening and early detection of pre-invasive lesion.
- Proper treatment and follow up of CIN.
- Avoid smoking
- If hysterectomy is done it should be total to avoid stump carcinoma.

II- Lines of treatment:

1- Surgical treatment:

■ The operation performed is either:

- Conization (fertility preservation)/Extrafascial total abdominal hysterectomy (only stage Ia₁).
- Modified radical hysterectomy (Wertheim operation).
- Radical hysterectomy (Meigs' operation).

Indications: **Stage I and Ia.**

Contraindications: **Stages IIb-IV (more parametrial involvement).**

The following structures are removed in radical hysterectomy:

- Uterus and cervix.
- Both tubes and ovaries (ovaries may be conserved in young women).
- Upper part of vagina.
- Parametrium (as much as possible).
- Pelvic lymph nodes (common, external, internal iliac, obturator and sacral).

■ Advantage of surgery:

- Some tumors are radioresistant.
- Recurrence after radiotherapy.
- Ovary can be preserved in young patients (< 35 y).
- Complication of radiotherapy are avoided.
- Can be done with associated pelvic pathology (fibroid, ovarian tumor).
- Can be done with pelvic infection.

■ Complications:

- Bladder dysfunction (most common) due to interruption of nerve supply to bladder. However, normal function usually returns within 1-3 weeks.
- Ureteric fistula (most serious): 1-2% mainly due to ischaemic necrosis or sometimes due to direct injury.
- DVT and pulmonary embolism.
- Lymphedema (15-20%) after pelvic lymphadenectomy.

N.B.: Radical vaginal trachellectomy can be done in young cases with stages Ib1 <2 cm where the cervix is removed vaginally followed by laparoscopic lymphadenectomy.

2- Radiation therapy:

■ Indications: either primary or adjuvant to surgery.

■ Contraindications:

- Radioresistant types
- Recurrent after previous irradiation and Very advanced cases with fistula
- Pregnancy.
- Pelvic infection.
- Associated condition: vaginal stricture, prolapse, fibroid, ovarian swelling.

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- **Complications:** Proctitis (diarrhea), bone marrow suppression and flaring up infection
 - **Technique:** The technique involves the use of :
 - **Intracavitary radiotherapy** (brachytherapy) for the tumour.
 - **External beam therapy** (teletherapy) by using the linear accelerator to treat the pelvic spread.
 - **Adjustment of the dose:** The radiation dose is adjusted to be directed to:
 - Point A: 2 cm lateral to central axis of the uterus and 2 cm above the above lateral fornix (dose for tumour)
 - Point B: 3 cm lateral to point A (dose for LN)
 - 3- **Chemotherapy:** Acts as Radiation sensitizer.
 - 4- **Palliative treatment:** Indicated in stage IV and recurrent cases.
 - **Palliative radiotherapy.**
 - **Palliative surgery :**
 - 1- **Pelvic exenteration:**
 - Anterior exenteration : If bladder is involved.
 - Posterior pelvic exenteration : if rectum is involved
 - Total pelvic exenteration: when bladder and rectum is involved.
 - 2- **Implantation of ureter into sigmoid colon or ileal loop in case of vesico-vaginal fistula and colostomy for recto-vaginal fistula.**
 - 3- **Laser, diathermy, cryocautery for fungating masses and local recurrence.**
 - **Other palliative measures :**
 - 1- **Measures to relieve pain:**
 - Drugs: pethidine – morphine.
 - Intrathecal injection of alcohol.
 - Pre-sacral neurectomy.
 - 2- **Blood transfusion and vaginal pack “in severe bleeding”.**
 - 3- **Proper diet and parenteral nutrition.**
 - 4- **Psychotherapy.**
- Prognosis:**
- “5-year survival rate” is:**
- | | | |
|-------------|------------|------------|
| - IA → 99% | - IB → 80% | - II → 70% |
| - III → 50% | - IV → 20% | |

Prognostic factors:

- L.N involvement and lymphovascular space invasion
- Parametrial involvement.
- Extent of tumor (stage).
- Tumor size.
- Depth of invasion.
- Tumor grade.
- Immunity of the patient.

Summary of treatment:

Stage I:

Stage Ia (Microinvasive or preclinical carcinoma)

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Do cone biopsy, then:

- If invasion is ≤ 3 mm in depth and ≤ 7 mm in width (**Ia1**) (risk of LN involvement $< 1\%$) do:
 - TAH or VH if the patient completed her family.
- Cervical conization if the patient desires to maintain fertility.
 - If invasion is between 3-5 mm in depth and 7 mm in width (Ia2), (the risk of LN involvement is approximately 5%) do: Modified radical hysterectomy.

Stage Ib or IIa (no obvious parametrial involvement):

- Radical hysterectomy (Meig's operation) Or
- Radiotherapy.

Stage IIb (obvious parametrial involvement): Radiotherapy .

Stage III: Radiotherapy.

Stage IVa:

- Radiotherapy Or Pelvic exenteration (rarely) if vesicovaginal or rectovaginal fistula + palliation.

Stage IVb: Radiotherapy + Chemotherapy for the distant metastasis + palliation

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Endometrial hyperplasia

It is a condition characterized by non-physiological, noninvasive endometrial proliferation due to prolonged unopposed estrogen effect as in cases of PCO, Estrogen producing tumor, ERT and Tamoxifen therapy.

Classification:

Simple hyperplasia (cystic glandular hyperplasia):

- Hyperplasia affects glands and stroma with cystic dilatation of glands.
- Variation in size of glands gives "Swiss cheese" appearance.
- It progress to malignancy in 1% of cases.

Complex hyperplasia (Adenomatous hyperplasia):

- Glands are increased in number and crowded with no or little intervening stroma.
- Malignant change occurs in 3 % of cases.

Atypical hyperplasia:

- Simple hyperplasia with atypia.
- Complex hyperplasia with atypia.
- Nuclei show atypia (irregular in size, shape, dense chromatin, clumping, large nuclei and ↑ N/C ratio).
- Progression to carcinoma 20 - 25 %.

N.B.: Recent terminology of endometrial hyperplasia:

- 1- **Hyperplasia:** Corresponds to simple and complex hyperplasia.
- 2- **Endometrial intraepithelial neoplasia (EIN):** corresponds to atypical hyperplasia.

New classification

The revised 2014 World Health Organization (WHO) classification is recommended. This separates endometrial hyperplasia into two groups based upon the presence of cytological atypia: i.e.

- (i) hyperplasia without atypia and (ii) atypical hyperplasia.

Diagnosis:

- Clinically: menorrhagia, irregular uterine bleeding, post-menopausal bleeding.
- U/S: increased endometrial thickness
- Hysteroscopic biopsy.
- Uterine curettage and histopathological examination.

Treatment: According to age and type of hyperplasia:

(A) Simple and complex hyperplasia without atypia:

- **Young woman: "conservative":**
- Both continuous oral and local intrauterine (levonorgestrel-releasing intrauterine system [LNG-IUS]) progestogens are effective in achieving regression of endometrial hyperplasia without atypia.
- The LNG-IUS should be the first-line medical treatment because compared with oral progestogens it has a higher disease regression rate with a more favorable bleeding profile and it is associated with fewer adverse effects.

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- Continuous progestogens should be used (medroxyprogesterone 10–20 mg/day or norethisterone 10–15 mg/day) for women who decline the LNG-IUS.
- Cyclical progestogens should not be used because they are less effective in inducing regression of endometrial hyperplasia without atypia compared with continuous oral progestogens or the LNG-IUS.
- **Postmenopausal: Hysterectomy.**

(B) Atypical hyperplasia:

- **Young woman:** - Conservative as above *or*
- Progesterone : continuous large dose norethisterone 20 mg/day for 6 months.
- **Woman > 40 years and postmenopausal woman: Hysterectomy. or**
In cases unfit for surgery or refusing it we can use Megesterol acetate 80 mg/day continuously.

Endometrial carcinoma

Definition: Malignant change of endometrium.

Incidence: It is the commonest invasive malignancy of female genital tract. It is common in:

Age: Average age is 55-70 years.

Race: Jewish-white women.

Parity: Nullipara and low parity.

Socioeconomic level: High SEL.

Positive family history.

Etiology: Unknown, the following are risk factors:

- **Hypoestrogenism:** Prolonged unopposed estrogen is the main risk factor:
 - Early menarche.
 - Delayed menopause.
 - Estrogen producing ovarian tumor.
 - PCO "polycystic ovary".
 - Prolonged ERT.
- It is commonly associated with diseases of excess estrogen: endometrial hyperplasia, endometriosis, fibroid.
- **Diabetes mellitus:** 10-30% are diabetic. Hyperinsulinemia is associated with ↑ insulin like growth factor I activity in the endometrium (thought to have neoplastic potential).
- **Obesity:** Due to peripheral conversion of androstenedione to E1 in fat.
- **Corpus cancer syndrome:** Association of DM, obesity, and HPN with endometrial cancer.
- **Genetic Factor:** There is familial tendency to develop endometrial cancer specially if there is history of breast cancer or Lynch II syndrome.
- **Chronic liver disease:** ↑ level of estrogen as it is metabolized in the liver.
- **Tamoxifen therapy:** When used for more than 5 years increases the risk of endometrial hyperplasia, polyp and carcinoma (2-3 folds).

Precancerous lesions:

(a) Endometrial hyperplasia:

- Simple hyperplasia: 1% risk of malignancy.
- Complex hyperplasia: 3% risk of malignancy.
- Atypical hyperplasia: 20-25% risk of malignancy.

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(b) Endometrial polyp:

Arise from basal layer of endometrium. It shouldn't be confused with endometrial cancer as only 0.5% of polyps are associated with endometrial carcinoma in post-menopausal woman.

Pathology:

Site: Usually arise in the fundus and tends to remain localized.

Macroscopic picture:

- **Localized type:** tumor appears as localized mass which become polypoidal.
- **Diffuse type:** large area of endometrial surface which appear as fungoid growth with surface ulceration and necrosis.

Microscopic picture:

- **Adenocarcinoma:** 90% of cases.
 - Classic type (Endometrioid adenocarcinoma).
 - Mucinous adenocarcinoma.
 - Papillary serous adenocarcinoma.
 - Clear cell adenocarcinoma.
- **Adenoacanthoma:** Adenocarcinoma + foci of benign squamous metaplasia.
- **Adenoacanthoma:** Adenocarcinoma + squamous cell carcinoma.
- **Squamous cell carcinoma** arises on top of squamous metaplasia as in cases of endometritis and pyometra.
- **Poorly differentiated carcinoma.**



Types of endometrial carcinoma:

| | Type I | Type II |
|------------------------------------|---------------------------------|--|
| Menopausal status | Premenopausal or perimenopausal | Postmenopausal |
| Estrogen related | Yes | No |
| Estrogen or progesterone receptors | Present | Absent |
| Histology of adjacent endometrium | Hyperplastic | Atrophic/ cystic polyp |
| Precursor lesions | Atypical hyperplasia | EIC |
| Grade | Low | High |
| Histologic subtype | Endometrioid | Serous carcinoma Clear cell carcinoma |
| Clinical behavior | Indolent | Aggressive |

Spread:

Direct spread "slow":

- The tumor invades myometrium slowly till reach peritoneal coat (several years) due to polysaccharide barrier in uterine wall, it is considered (surface rider).
- Extension to cervix.
- Extension to tubes, ovary and surrounding structures.

Lymphatic spread "late":

- Upper 1/3: Along ovarian lymphatics to paraaortic L.N.
- Middle 1/3: Internal iliac L.N.
- Lower 1/3: Like cervical carcinoma.
- Cornu: Along lymphatics in round ligament to superficial inguinal L.N.
- Retrograde lymphatic spread: Vaginal vault and vulva.

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Blood spread: (Late)

- Liver, lung, bone and brain.
- Retrograde vascular spread to suburethral area of anterior vaginal wall.

Seedling (surface implantation):

- Vaginal vault after hysterectomy is the commonest site for recurrence (10%).

Staging and grading:

| Revised FIGO staging for carcinoma of endometrium, 2009 | |
|--|--|
| Stage I* | Tumor confined to the corpus uteri |
| IA* | No or less than half myometrial invasion |
| IB* | Invasion equal to or more than half of the myometrium |
| Stage II* | Tumor invades cervical stroma, but does not extend beyond the uterus** |
| Stage III* | Local and/or regional spread of the tumor |
| IIIA* | Tumor invades the serosa of the corpus uteri and/or adnexae *** |
| IIIB* | Vaginal and/or parametrial involvement *** |
| IIIC* | Metastases to pelvic and/or para-aortic lymph nodes*** |
| IIIC ₁ * | Positive pelvic nodes |
| IIIC ₂ * | Positive para-aortic lymph nodes with or without positive pelvic lymph nodes |
| Stage IV* | Tumor invades bladder and/or bowel mucosa, and/or distant metastases |
| VIA* | Tumor invasion of bladder and/or bowel mucosa |
| VIB* | Distant metastases, including intra-abdominal metastases and/or inguinal lymph nodes |
| *Either G1, G2, or G3. Grade 1: 5% or less of a solid growth pattern (Highly differentiated) Grade 2: 6% to 50% of a solid growth pattern (Moderately differentiated) Grade 3: More than 50% of a solid growth pattern (Poorly differentiated) **Endocervical glandular involvement only should be considered as Stage I and no longer as Stage II. ***Positive cytology has to be reported separately without changing the stage. | |

Diagnosis:

Symptoms:

- **Vaginal bleeding:** The most common complaint either:
 - Post-menopausal bleeding (75%).
 - Perimenopausal bleeding.
- **Vaginal discharge:**
 - It starts watery, then blood stained, offensive.
 - Occasionally patient passes a piece of polypoidal growth per vagina.
 - Cases with cervical extension, obstruction may occur and pus collects inside the cavity leading to pyometra.
- **Pain:**
 - Late symptom, due to spread to peritoneum, pyometra or extra uterine spread.
 - Simpson pain: Suprapubic colicky pain due to expulsive contractions.
- **Symptoms of complications:**
 - Cachexia, peritonitis, etc.

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Signs:

- **General examination:** DM, obesity, supraclavicular and inguinal L.N.
- **Abdominal examination:** Masses, ascites, palpable lymph nodes...etc.
- **Pelvic examination:**
 - Inspection of para-urethral and suburethral area.
 - P/V to detect spread to cervix and vagina.
 - Bimanual examination:
 - The uterus may be:
 - Normal sized "slowly growing tumor".
 - Small sized "post-menopausal atrophy".
 - Enlarged in size pyometra or associated fibroid (30% of cases).
 - Palpation of ovary: (Granulosa cell tumor – metastasis):
 - Speculum examination: To detect spread to cervix and vagina
 - P/R:
 - Spread to rectum.
 - Examination of parametrium.

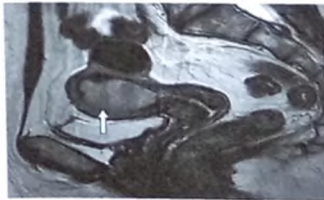
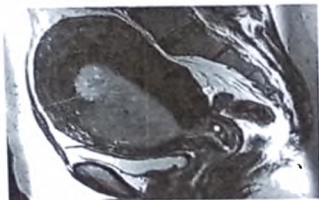
Investigations:

Imaging:

1. **Transvaginal U/S:** Endometrial thickness > 4mm in post-menopausal suggest endometrial abnormality. U/S can delineate the lesion and detect degree of myometrial invasion.



2. **MRI/CT** can detect accurately degree of myometrial invasion, lymphatic spread and enlarged L.Ns, lung, bone and liver spread.



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Endometrial biopsy:

Endometrial biopsy and Histopathological examination is the only method for accurate diagnosis. It must be done in every woman with post-menopausal bleeding or > 40 y with abnormal uterine bleeding.

Methods:

1. **Office endometrial biopsy:** By Novak curette, Vabra aspiration or pipelle suction curette.
 - **Advantages:** Done without anesthesia, Less cost, Less complication.
 - **Diagnostic accuracy** is 92 -98% → replaced curettage and become 1st step in making diagnosis.
2. **Hysteroscopic directed biopsy.**
3. **Fractional curettage:** Three separate specimens from cervical canal, isthmus and body of uterus.
 - In case of endometrial carcinoma: the obtained material is plentiful, cheesy, friable and necrotic with Failure of uterine wall to grate (silent curettage).
 - Small growths are missed in 10% of cases.



Hysteroscopy:

The most reliable methods for diagnosis. It is used to inspect uterine and cervical cavity, determine extent of growth. It may be followed by curettage or directed biopsy.

Metastatic workup: Cystoscopy, proctoscopy, IVU, chest x-ray and bone scan.

Preoperative investigations:

CBC, blood sugar, urine analysis, liver function, kidney function and ECG.

D.D:

- Causes of post-menopausal bleeding.
- Causes of perimenopausal bleeding.
- Causes of pyometra.

Treatment of endometrial carcinoma:

Prophylactic treatment:

- ERT given to postmenopausal women should be combined with progesterone.
- Proper treatment of chronic anovulation (PCO), endometrial hyperplasia and endometrial polyp.
- Endometrial biopsy should be done for every case above 40 years with abnormal uterine bleeding to exclude EC.
- Follow up for women with risk factors e.g Tamoxifen therapy and family history

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Treatment of established cases:

Surgery: Staging laparotomy is the primary treatment and consists of:

- **Incision:** most common vertical midline.
- **Cytologic examination** of peritoneal washing or ascitic fluid.
- **Exploration** of pelvis and abdomen.
- **Hysterectomy** and bilateral salpingo-oophorectomy.
- **Bilateral pelvic and para-aortic lymphadenectomy** (ACOG 2005), however this is a point of controversy as some don't recommend it.
- **Complete infracolic omentectomy** and peritoneal biopsies in cases of:
 - Clear cell adenocarcinoma.
 - Papillary serous adenocarcinoma.

According to staging laparotomy, adjuvant therapy will be given as follows:

1. **Stage I:**
TAH + BSO (panhysterectomy) seems to be sufficient except if there is myometrial invasion >1/2 myometrium, poorly differentiated (G3) or non-endometrioid type. These cases necessitate further lymphadenectomy or adjuvant radiotherapy.
2. **Stage II:**
- **Standard therapy** is modified radical hysterectomy + pelvic lymphadenectomy + postoperative radiotherapy.
3. **Stage III:**
- **If diagnosed before surgery:**
 - Radiotherapy "uterine cavity" and vaginal vault are packed with radium or cesium "followed by external pelvic irradiation.
 - Then TAH+BSO if tumor is resectable + post-operative radiotherapy.
- **If diagnosed during surgery:**
 - TAH + BSO "if tumor is resectable" - pelvic lymphadenectomy + Biopsy from suspected areas and omentum, followed by adjuvant postoperative radio therapy.
4. **Stage IV:**
IVa: Pelvic exenteration in selected patients + radiotherapy.
IVb:
 - Hormonal therapy.
 - Chemotherapy.
 - Radiotherapy.

Radiotherapy for endometrial carcinoma:

Endometrial carcinoma (endometrioid type) is radiosensitive tumor however 5-year survival rate is better with surgery than radiotherapy. So, radiotherapy is 2nd choice after surgery in treatment of endometrial carcinoma and used in:

- Patients unfit for surgery.
- Adjuvant therapy.
- Palliative in recurrent and advanced cases.

Types of radiotherapy:

- **Internal irradiation:** Cesium and radium.
- **External irradiation.**
- If para aortic L.N are involved: Extended field radiation.

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Hormonal therapy for endometrial carcinoma:

- Many endometrial carcinomas are hormones receptor positive and are estrogen dependent "80%".
- Drugs are:
 - Medroxy progesterone acetate.
 - LHRH analogues.
 - Danazol – androgen.
 - Gestrinone.

N.B: In papillary serous EC, chemotherapy is the proper adjuvant treatment (like ovarian cancer).

Palliative treatment:

1. **Palliative surgery:** Pelvic exentration.
2. **Palliative radiotherapy.**
3. **Palliative chemotherapy / hormonal treatment.**
4. **Others:** Relief pain, blood transfusion, proper nutrition and psychotherapy.

Prognostic factors:

- FIGO stage: The most important. It includes
 - Myometrial invasion.
 - Lymphovascular space invasion.
- Histologic cell type and grade.
- Hormonal receptors.

*The overall prognosis of endometrial carcinoma is better than cervical carcinoma as the majority of cases (75%) discovered in stage I.

This good prognosis is because the tumor is usually well differentiated, slowly growing. Late Lymphatic spread and being hidden with uterine cavity away from infection.

* 5-year's survival rate is:

- Stage I: 80-90%.
- Stage II: 60-70%.
- Stage III: 30-40%.
- Stage IV: 0-20%.

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Uterine Sarcoma

Definition:

Malignant tumor arising from any mesodermal tissue of the uterus e.g.: muscle.

Incidence:

Rare tumor (1-3% of malignant uterine tumors).

Risk factors:

- The same as endometrial carcinoma.
- History of previous radiation of pelvis in 20% of cases.

Classification:

It may arise at body of uterus or cervix.

Pure mesenchymal tumour:

- **Smooth muscles:**
 - Leiomyosarcoma.
 - Smooth muscle tumour of unknown malignant potential (STUMP).
- **Endometrial stromal tumors:**
 - - Endometrial stromal nodules.
 - - Endometrial stromal sarcoma.
 - - Undifferentiated sarcoma.

Mixed epithelial and mesenchymal:

- **Malignant mixed mesodermal tumor (MMT): carcino-sarcoma.**
- **Adenosarcoma.**

Spread:

Like endometrial carcinoma but spread **mainly by blood stream**.

Staging:

Like endometrial carcinoma

I: Limited to body of uterus.

II: Infiltration of cervix.

III: Extra uterine but still within pelvis.

IV: Tumor spread to bladder or rectal mucosa or distant spread.

Diagnosis:

● Symptoms :

- Bleeding: main symptoms.
- Vaginal discharge.
- Pain.
- Cachexia.

● Signs:

- Like endometrial carcinoma but uterus is enlarged on > 50% of cases.
- Presence of polyp protrudes from cervix.

● Investigations:

- Endometrial biopsy.
- TVS.
- MRI and CT.
- Metastatic work up (chest x-ray, liver and bone scan).

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Treatment:

- Surgically fit: Total abdominal hysterectomy + bilateral salpingo-oophorectomy and pelvic lymphadenectomy. Then radiotherapy + chemotherapy.
- Surgically unfit: radiotherapy + chemotherapy + palliative.

N.B.: In leiomyosarcoma, no lymphadenectomy is needed.

Prognosis:

- Poor prognosis.
- Better prognosis with leiomyosarcoma.

Leiomyosarcoma

The commonest type:

- Arise *de novo*.
- On top of fibroid (0.1%).

C/P:

Criteria of malignant change in fibroid:

- Rapid growth.
- Rapid recurrence.
- Post-menopausal growth.
- Post-menopausal bleeding and pain.
- Cachexia.
- Soft consistency.

At operation:

- Infiltration of capsule.
- - Loss of whorly appearance.
- - Hemorrhage and necrosis.

N.B. Number of mitotic figures is the single most accurate characteristic to differentiate leiomyoma from leiomyosarcoma.

- If M.F < 5/10HPF → Benign.
- If M.F 5-9/10HPF → STUMP (smooth muscle tumor of unknown malignant potential).
- If M.F > 10/10HPF → malignancy regardless presence or absence of cellular atypia.

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Sarcoma botryoides (Grape like sarcoma)

- It is rhabdomyosarcoma arise from subepithelial connective tissue of vagina or cervix.
- It usually occurs in children and infants (<3y).

Clinically:

- Soft pinkish polyps resemble a bunch of grape.
- It grows rapidly and may appear at vulva.
- It causes vaginal bleeding and may be mistaken for precocious puberty.

Microscopically:

Formed of embryonal rhabdomyoblast + undifferentiated cells + myxoid like ground substance.

Treatment:

- Combination chemotherapy (VAC): Vincristine, Adriamycin, Cyclophosphamide.
- Radiotherapy (if tumor persist).
- Surgery (total vaginectomy + radical hysterectomy).
- 5-y survival rate is 80%.

Gestational choriocarcinoma

Definition: Highly malignant gestational trophoblastic tumor (producing a large amount of HCG).

Incidence: In Far East 1/4000, in U.S.A. 1/40 000.

Origin:

- 50% follows vesicular mole.
- 25% follows abortion
- 23% follows normal pregnancy.
- 2% follows ectopic pregnancy.

Clinical classification of malignant gestational trophoblastic neoplasia (GTN):

- 1- Non metastatic: confined to the uterus.
- 2- Metastatic.

Prognostic classification:

- Low risk group (Good prognosis): with no risk factors.
- High risk group (Bad prognosis): with one or more of the following risk factors:
 - H.C.G. level in serum > 40,000 mIU / ml.
 - Duration of the disease > 4 months.
 - Following full term pregnancy.
 - Brain and liver metastasis.
 - Failure of previous chemotherapy.

Pathology:

Macroscopic Picture:

• The uterus:

- Localized type: which may grow to form polypoidal growth.
 - Diffuse type (affecting the whole uterine cavity).
 - Intra-mural type (invades the myometrium not appearing on the endometrial surface). this type shows no bleeding, negative curettage in spite of very high.
 - H.C.G. level.
- In all types:** lesion is dark red, hemorrhagic, friable and necrotic.

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- **The ovaries:**

- May be the site of metastasis.
- May show theca lutein cysts in 20% of cases (due to hyperstimulation: high HCG. see ovarian tumors).

Microscopic Picture:

- **Choriocarcinoma:**

- Sheets of malignant trophoblasts (catotrophoblasts and syncytio-trophoblast cells) with blood lakes.
- Absent villous pattern: is the most characteristic sign.

- **Ovarian cysts:** Lined with theca lutein cells.

Spread:

- Direct Spread: to the myometrium, tubes, ovaries etc.
 - Blood spread: (the most common and earliest)
 - Lung secondaries (75%), liver, brain and bone.
 - Retrograde venous spread to vulva and vagina.
 - Lymphatic Spread:
 - From uterine body: as endometrial carcinoma (see before).
 - From isthmus or cervix: as cervical carcinoma (see before).
- The commonest sites for metastasis are: lungs (80%), vagina (30%), liver (10%), and brain (10%).**

Complications:

- General Complications: Cachexia, haemorrhage, infection and spread.
- Specific Complications: as complications of vesicular mole
 - Shock (due to severe bleeding).
 - Infection.
 - Perforation .

Staging:

- Disease confined to the uterus.
- Disease extends outside the uterus but limited to the genital structures.
- Disease extends to the lung with or without known the genital tract involvement.
- All other metastatic sites.

Diagnosis:

Symptoms:

- Persistent Uterine Bleeding after an event of pregnancy e.g. evacuation of vesicular mole.
- Offensive vaginal discharge due to ulceration and infection.
- Abdominal or vaginal swelling.
- Symptoms of Spread; e.g. Hemoptysis (lung secondaries) may be the 1st presentation or complication: acute abdomen in perforation.

Signs:

- **General Examination:**

- To assess the general condition; Cachexia, anemia etc.
- To detect distant metastasis.
- Hyperthyroidism in 10% of cases.
- Fever due to infection and necrosis.

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- **Abdominal examination:** Palpate the liver for metastasis.

- **Local Examination:**

- Vulva and vagina: Hemorrhagic nodules.
- Uterus: Normal sized or enlarged.
- Ovaries: Cystic and enlarged.

Investigations:

- **Investigations to Screen Early Cases:**

In cases of vesicular mole: proper follow up by H.C.G. level after evacuation.

- **Investigations to confirm the diagnosis:**

- B- H.C.G. level in serum by R.I.A.: very sensitive test.
- Dilatation and Curettage: the specimen shows microscopic picture of choriocarcinoma but may be negative (in the intra-mural type) so the B- H.C.G. is more important.
- Biopsy from metastasis in the vulva and vagina.

- **Investigations to certify the spread:**

- Ultrasonography: to detect the tumor, to diagnose ovarian cysts and to detect liver metastasis.
- Doppler ultrasound: to detect intramural choriocarcinoma.
- CT scan or MRI (pelvi-abdominal):
 - * To detect the extent of myometrial invasion.
 - * To detect secondaries e.g. liver metastasis.
- Chest x-ray: to exclude metastasis in the lungs (80%): Canon balls. If negative: CT chest.
- Lumbar puncture: measure CSF HCG/ serum HCG level
 - * Normally: < 1: 60
 - * If > 1: 60 brain metastasis.

Differential diagnosis:

- Causes of post-abortive bleeding.
- Causes of 2ry post-partum hemorrhage.
- From ectopic pregnancy.

Treatment:

Prophylactic treatment: Early diagnosis = proper screening (see before).

Active treatment → Chemotherapy

1. Plan of treatment: (according to the prognostic classification)

- **Low risk group:**

- Single Agent Chemotherapy

- ⇒ If there is response, repeat the course after the patient recovers from toxic symptoms (after 10 days). Repeat till HCG level becomes undetected. Then one more course is added.
- ⇒ If there is no response, deal as high risk group.

- **High risk group:**

- Multiple Agent Chemotherapy:

- ⇒ If there is response, repeat the course after the patient recovers from toxic symptoms (after 10 days). Repeat till H.C.G. level becomes undetected. Then 3 more courses are added.
- ⇒ If there is no response, think of resistant nodules, detect their sites then treat accordingly e.g. liver metastasis; 2000 RAD irradiation.

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2. Lines of treatment:

A. Chemotherapy:

• **Single Agent (Methotrexate)**

- **Indications:**

- ⇒ In cases of non-metastatic choriocarcinoma and metastatic with good prognosis.

- **The mode of action:**

- ⇒ Inhibits dihydrofolate reductase enzyme that converts folic acid into fulminic acid (the active form) which is necessary for DNA and RNA synthesis.

- **The routes of administration:** Oral, IM. Injection, IV. injection.

- **The regimen:** The most commonly used protocol is the 8 day alternating:

- ⇒ Methotrexate; 1 mg / kg B.W. on alternating days (1, 3, 5, 7).
- ⇒ Folinic acid (Citrovorum factor); 0.1 mg/Kg B.W. every other day (2, 4, 6, 8).

- **Side effects:**

- ⇒ 1. Bone marrow depression (pancytopenia).
- ⇒ 2. Liver and kidney toxicity.
- ⇒ 3. Mucous membrane ulceration: GIT ulceration.
- ⇒ 4. Skin pigmentation and alopecia.

• **Combination Chemotherapy**

- **Indication:** In metastatic cases of choriocarcinoma with bad prognosis.

- **The commonly used combination are:**

- ⇒ Triple therapy of LI: "MAC" = (Methotrexate + Actinomycin-D + Cyclophosphamide).
- ⇒ Modified Bagshaw protocol: "EMA-CO" = (Etoposide + Methotrexate + Actinomycin-D + Cyclophosphamide + Oncovin" vincristine").

B. Surgical treatment: (hysterectomy)

• **Indications:**

1. Age above 40 years and completed her family.
2. Drug resistance or toxicity.
3. Complications: sever bleeding, perforation of the uterus.
 - ⇒ The operation is done during the course of chemotherapy.
 - ⇒ Also, removal of localized masses in the vagina, lung, brain that persist after chemotherapy.

For liver metastasis; radiotherapy 2000 RAD

For brain metastasis: intrathecal methotrexate or radiotherapy 2000 -3000 RAD

Follow up:

- Successful treatment = HCG remains negative for 3 successive weeks.
- HCG is measured every week for 6 weeks, then every 2 weeks for the rest of the first year.
- Then every month for the second year, then every 3 months for 5 years, then every 6 months for life.
- Oral contraceptive pills should be used for 1 year.

Prognosis:

- About 97% cure rate in low risk group.
- 80% in high risk group.

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Placental site trophoblastic tumor

- The tumour is very rare, and is the rarest form of GTT.
- It arises from placental site after any form of pregnancy.
 - The majority (95%) follow a full-term delivery.
 - Few cases follow abortion or hydatidiform mole.
- The tumor consists of intermediate trophoblastic cells invading the myometrium. The intermediate trophoblast is not differentiated into cyto- or syncytiotrophoblast.
- The tumor is locally malignant and may perforate the uterus.
- Distant metastases are rare (15%).
- Patient presents with either amenorrhoea or abnormal vaginal bleeding and uterine enlargement.
- The cells secrete small amounts of HCG so the HCG level is normal or low usually < 3000 mIU/ml. The human placental lactogen may be elevated as some of the cells secrete this hormone.
- The treatment is hysterectomy.
- The tumor is generally resistant to chemotherapy

Non-neoplastic ovarian swellings (tumor-like conditions)

- 1- Functional ovarian cysts:** The most frequent cyst of the ovary.
They result from fluid distension into one of natural constituents of the ovarian cortex. Its size is usually <6 cm and regress spontaneously. It is managed by follow up or may need suppression by oral contraceptive pills. No surgical interference is needed except if >6 cm, persist >2 months or if complicated.

Follicular cyst:

- Due to failure of Graafian follicle to rupture and become cystic under effect of gonadotrophins.
- Characters:
 - Small size < 5 cm.
 - Contain clear fluid.
 - Lined by granulosa cells.
 - Resolve spontaneously.
- Produce high amount of estrogen.

Corpus luteum cyst:

- Cyst develops in corpus luteum of pregnancy or without pregnancy.
- It is a small cyst (< 5 cm) contain yellowish fluid.
- C/P: It secretes progesterone with short period of amenorrhea.
- When regress, withdrawal bleeding.
- Bimanual examination → unilateral adnexal swellings.
- U/S → cyst and by Doppler (ring of fire appearance).
- Complications: It is highly vascular. If ruptured → internal hemorrhage and acute abdomen (DD: ectopic pregnancy).
- Laparotomy may be required only if internal hemorrhage occurred.

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Theca-lutein cyst:

- Multiple cysts, may reach large size.
- Lined by luteinized theca cells in response to excessive HCG stimulation.
- **Etiology:**
 - Vesicular mole and choriocarcinoma
 - Ovarian hyperstimulation syndrome.
- **Fate:** it usually regresses spontaneously.
- **Treatment:** it requires no treatment unless complicated.

2- Polycystic ovarian disease.

3- Endometriotic cyst (chocolate cyst).

4- Inflammatory cyst (tubo-ovarian cyst or tubo-ovarian abscess).

5- Hemorrhagic cyst "hemorrhage in any type of cyst".

6- Inclusion cyst:

- Surface epithelium of ovary may be invaginated during ovulation and forming cyst near surface of ovary.
- Usually, multiple, small, near menopause.
- Fate remains quiescent or form neoplasm of epithelial origin.

7- Pregnancy luteoma:

- Solid-ovarian swelling in response to normal HCG level.
- It may reach large diameter during pregnancy (16 cm).
- It usually regress spontaneously after labor.
- MIC "nodular mass of luteinized cells".
- It produces "androstenedione"; virilization of the mother. the female fetus is not affected due to change of androgen into estrogen in the placenta (aromatase). Virilization signs regress spontaneously.

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Ovarian tumors

"WHO classifications of ovarian tumors"

I- Epithelial tumors:

Serous tumors:

- Benign.
- Border line "low malignant potential".
- Malignant.

Mucinous tumors:

- Benign.
- Border line "low malignant potential".
- Malignant.

Endometrioid tumors:

- Benign.
- Border line "low malignant potential".
- Malignant.

Mesonephroid (clearcell) tumors:

- Benign.
- Border line "low malignant potential".
- Malignant.

Brenner tumor:

- Benign.
- Borderline and malignant (very rare).

Unclassified epithelial tumor.

II- Sex cord stromal tumors:

Granulosa-stromal tumors:

- Granulosa cell tumor.
- Thecoma-fibroma group:
 - a- Thecoma.
 - b- Fibroma.
 - c- Unclassified.

Androblastoma (Sertoli-Leydig cell tumor):

- Well differentiated:
 - a- Sertoli cell tumor.
 - b- Sertoli-Leydig tumor.
 - c- Leydig cell tumor (Hilus cell tumor).
- Moderately differentiated.
- Poorly differentiated.
- With heterologous element.

Gyandroblastoma.

Unclassified.

III- Germ cell tumor:

Undifferentiated (dysgerminoma).

Differentiated:

- Extra-embryonal:
 - a- Endodermal sinus tumor (from yolk sac).
 - b- Choriocarcinoma (from trophoblast).

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- Embryonal:
 - Teratoma:
 - Immature.
 - Mature:
 - * Solid.
 - * Cystic; dermoid cyst (mature cystic teratoma).
 - Monodermal and highly specialized:
 - * Struma ovarii.
 - * Carcinoid.
 - * Struma ovarii and carcinoid.
 - * Others.
 - Embryonal carcinoma.
 - Polyembryoma.

IV- Gonadoblastoma.

VI- Unclassified tumors.

VII- Metastatic (2ry) tumors.

Pathology of different ovarian swellings:

Primary ovarian tumours

(A) Epithelial ovarian tumors:

- It represents 80% of all ovarian tumors and 90% of malignant ovarian tumors.
- It arises from surface epithelium (coelomic epithelium).
- It may be benign, borderline, malignant.
- Irritation of epithelium may give any type of tissue arising from coelomic epithelium.
 - Tubal like epithelium → serous tumors.
 - Cervical like epithelium → mucinous tumors.
 - Endometrial like epithelium → endometrioid tumors.
 - Mesothelial like epithelium → mesonephroid tumors.
 - Immature subepithelial cells → Brenner tumors.

I. Serous tumors:

- Commonest type of ovarian tumor.
- It may arise from invagination of surface epithelium.



Benign tumor: serous cystadenoma:

- It is the most common epithelial ovarian tumor.
- Unilateral → 90%, bilateral → 10%.
- MAC:
 - Unilocular thin translucent wall.
 - Smooth surface.
- MIC:
 - Lined by single layer of tubal like epithelium "ciliated, secretory cells".
 - Stroma is fibrous and contains: psammoma bodies "calcified degenerated epithelial cells".
 - Psammoma bodies are characteristic of serous epithelial tumors not for malignancy.

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Borderline tumors:

Bilateral: 25-40%.

MAC: They are generally multilocular and contain more papillae than benign tumors.

MIC:

- Lining epithelium is stratified (not more than 3 layer).
- Budding "loose cellular clusters are seen intracystic fluid".
- Malignant characteristics of cells.
- No invasion of Basement membrane.
- More psammoma bodies.

Malignant tumors:

- It is the commonest type of 1ry ovarian cancer.
- Suspected if:
 - Bilateral.
 - Solid tumor or partly cystic.
 - Ascites.
 - Cut section → hemorrhage and necrosis.
- MIC: clusters of malignant (tubal like epithelial) cells with stromal invasion.



II. Mucinous tumors:

- It is the 2nd common epithelial tumor.

Benign tumors: Mucinous cystadenoma:

- **Bilateral:** 5-10% of cases.
- **MAC:**
 - Cystic tumor. - May attain large size (56 kg was described).
 - Thin translucent wall with bluish hue with multilocular thin septae on cut section.
- **MIC:** Cyst is lined by tall columnar epithelium with goblet cells "resembling endocervix".
- **Pseudomyxoma peritonii:** Rupture of cyst, mucine spreads through peritoneal cavity. The epithelial cells are implanted on the peritoneum with continuous mucous production even after removal of tumor
 - Death may occur due to intestinal obstruction.
 - Treatment is removal of tumor, evacuation of mucinous material from abdomen, instillation of intraperitoneal cytotoxic agent or radiotherapy.

Borderline tumors:

- Similar to benign with more papillae.
- MIC: like borderline serous tumors.

Malignant tumors:

- More solid or partially cystic.
- MIC → criteria of malignancy + stromal invasion.

III. Endometrioid tumors:

Benign endometrioid tumors: resembles endometriosis.

Borderline tumors: Like benign but with malignant criteria and no stromal invasion.

Malignant tumors:

- MIC → glandular pattern resembling endometrial carcinoma.
- It is associated with endometrial carcinoma in 25% of cases "carcinoma ovarii et uteri".

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IV. Mesonephroid (clear cell adenocarcinoma):

- Almost malignant.
- Usually unilateral.
- MIC:
 - Cells are arranged in sheets or line glandular spaces.
 - Hobnail cells: hyperchromatic nucleus over which cytoplasmic membrane appear to be collapsed. Protrudes in the lumen.

V. Brenner's tumor:

- Majority of cases are benign.
- Small (3- 8cm), solid tumor.
- Gross appearance: like fibroma, white fibrous tumors.
- MIC: Nests of transitional like epithelium embedded in Dense fibrous stroma with Coffee-bean appearance of nuclei.

(B) Sex cord-stromal tumors:

- They arise from sex cords and ovarian stroma.
- They are composed of cells:
 - Female cell "Granulosa cell- theca cells".
 - Male cells "Sertoli cell- Leydig cell".

Granulosa-stromal tumors:

1. Granulosa cell tumors:

- MAC → Unilateral, solid, smooth, lobulated surface, variable size with yellow cut section.
- MIC:
 - Formed of granulosa cells which are rounded with scanty cytoplasm and large nuclei. It has coffee- bean cells.
 - Call-Exner bodies arranged in rosette fashion around central hyalinized area due to nuclear degeneration "pathognomonic".
- Behavior → Malignant "low grade".
- It is hormonally active secretes Estrogen and inhibin:
 - **Precocious puberty:** Before puberty.
 - **Irregular bleeding:** Reproductive life.
 - **Post-menopausal bleeding:** Post-menopausal.
- Prolonged unopposed E → Endometrial hyperplasia and carcinoma.

2. Fibroma (benign solid tumor):

- MAC:
 - Solid tumor with whorly cut section.
 - May have long pedicle.
- MIC → Bundles of spindle cells within dense C.T. stroma.
- Meig's syndrome → Benign solid ovarian tumor + ascites + right sided pleural effusion.
- Ascites due to:
 - Mechanical irritation of peritoneum by mobile tumor.
 - Loss of fluid from dilated veins on surface.
 - Secretion by tumor cells.

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- Pleural effusion due to transfer of fluid from peritoneal cavity by lymphatics "right side".

NB: Pseudo-Meig's: malignant ovarian tumors+ ascites+ right sided pleural effusion.

3. Thecoma:

- Solid benign tumor.
- Usually develop after menopause.
- It secretes Estrogen: post-menopausal bleeding- endometrial hyperplasia or carcinoma.

Sertoli-Leydig tumor "androblastoma = arrhenoblastoma":

- It is of low-grade malignancy.
- **MAC:**
 - Unilateral in 95% of cases.
 - Solid tumor.
- **MIC:** composed of Sertoli cells arranged in seminiferous tubule like pattern and interstitial cells of Leydig "contains intracytoplasmic crystalloids of Rieck".
- Behavior is low-grade malignancy.

Gynadroblastoma:

- Very rare tumor.
- Composed of mixture of granulosa cells and Sertoli-Leydig cells.
- It may be androgenic or estrogenic.

(C) Germ cell tumors (5%):

- They arise from primordial germ cells.

Dysgerminoma:

- 2nd commonest type of germ cell tumor after teratoma.
- The commonest malignant germ cell tumor (2% of malignant ovarian tumors).
- Arise in streak gonads (gonadal dysgenesis).
- It gives early LN metastasis.
- It is the most radiosensitive ovarian tumor.
- **MIC:**
 - It is composed of primitive germ cells arranged in alveolar pattern and separated by CT stroma infiltrated by **lymphocytes**.
 - Sometimes contain syncytiotrophoblast.
- It is of low grade malignancy.
- **Tumor marker:** Lactate dehydrogenase (LDH).
- It usually arises in gonadal dysgenesis.

Teratoma:

- **Immature (malignant) teratoma:**

- It is the 2nd commonest malignant germ cell tumor.
- **MAC:**
 - Solid and may contain cystic area.
- **MIC:**
 - Mixture of embryonic cells of 3 germ layers.
 - Commonly neuroepithelial tissue.



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- Mature teratoma "Benign cystic teratoma – Dermoid cyst":

- It is the most common germ cell tumor.
- It is the commonest ovarian tumor in childbearing period and during pregnancy.
- **MAC:**
 - It is unilateral (bilateral 20%).
 - Unilocular.
 - Thick opaque wall.
 - Smooth outer surface.
 - Has long pedicle:
 - * Liable to torsion.
 - * Freely mobile "mouse of abdomen".
- **Contents:** Greasy sebaceous fluid, tuft of hair.
- Inner wall shows nodule or mammilla → Rokitsky protuberance; to which hair tuft is attached.
- The mammilla contains tissues of 3 germ discs.
- **It contains:** skin, skin appendages, teeth, bone, cartilage, GIT tissues and neural tissues.
- **MIC:**
 - Cyst is lined by stratified squamous epithelium
 - Structures found are "ectodermal, mesodermal, endodermal".
 - Malignant change (<1%) → any type of malignancy but commonly squamous cell carcinoma.
- **Mature solid teratoma:** Very rare.
- **Monodermal:**
 - **Struma ovarii:** It is solid Benign teratoma in which thyroid tissue predominate.
 - **Carcinoid tumor:** Contains predominant argentaffin cell which secretes serotonin (5HT).

Endodermal sinus tumor "yolk sac tumors":

- It is the most aggressive germ cell tumor.
- It arises from yolk sac endodermal cells.
- It secretes alpha-fetoprotein.

Chorio-carcinoma of ovary "non-gestational":

- Extremely rare, but highly malignant.
- It secretes large amount of HCG → may lead precocious puberty and irregular uterine bleeding.

Metastatic (2ry) ovarian tumors

- It constitutes 15- 20% of ovarian malignancy.
- Ovary is a very common site for metastasis.
- The 1st tumor may be:
 - Genital: Endometrial cancer, vulva, tube. It reaches ovary by direct spread, lymphatic, retrograde vascular.
 - Extragenital: Stomach and intestine.
- It reaches ovary by (Trans-coelomic spread- retrograde lymphatic- blood spread).
- Secondaries in ovary may be:
Typical: Similar to histological picture of 1st tumor.

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Atypical (Krukenberg tumor):

- 1^o tumor is in stomach, colon, breast, and gall bladder.
- **Mode of spread:** retrograde lymphatic.

- **MAC:**

- Bilateral.
- Solid.
- Large.
- Lobulated.
- Smooth surface.
- Intact capsule.
- Preserve shape of ovary.
- Cut section shows waxy consistency, greyish in color.



- **MIC:**

- Signet cells has large oval, rounded cells with eccentric nucleus and granular cytoplasm.
- Stroma is fibromyxomatous.

Complications of ovarian tumours:

(1) **Torsion:** (axial rotation)

The commonest complication (found in 12% of cases at operation).

Etiology:

(A) **Predisposing factors**

- 1- Moderate Size
- 2- Long pedicle
- 3- Smooth surface and absence of adhesions → freely mobile.
- 4- Abdominal tumor rotates easily than pelvic tumor.
- 5- Pregnancy: the growing uterus displaces the tumor.
- 6- Puerperium: due to
 - Laxity of abdominal wall.
 - Involution of the uterus → wider space.

NB: Torsion of ovarian tumors is very common during puerperium.

(B) **Precipitating (exciting) factors:**

- 1- Sudden movement of the patient.
- 2- Sudden contraction of the abdominal wall e.g. coughing
- 3- Movements of intestines e.g. diarrhea.
- 4- Contraction of uterus during labor.
- 5- Abdominal massage after delivery.

Sequelae of torsion:

(A) **Acute torsion:**

- Obstructs both arteries and veins → acute abdomen and tumor is necroed, tender and ↑ in size and even gangrene.

(B) **Gradual torsion:** Obstruction of veins and lymphatics at first:

- Congestion and hemorrhage inside the tumor.
- Lymphatic oozing leading to adhesions to omentum or intestine.
- Rarely → parasitic tumor.
- If torsion continues → obstructs arteries → necrosis and gangrene.

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C/P:

Symptoms:

- 1- Sudden onset of severe lower abdominal pain (acute abdomen).
- 2- Vomiting.

Signs:

- 1- The patient is shocked (neurogenic).
- 2- Tender, rigid lower abdomen.
- 3- The tumor: is tense and tender.

Investigations:

- 1- **Ultrasonography:** Stromal edema and displacement of follicles to the periphery (Bull's eye sign).
- 2- **Doppler Ultrasonography.**
- 3- **Laparoscopy.**

Treatment:

- 1- Antishock measures
- 2- Laparotomy and ovariectomy (removal of tumor + ovary) or ovarian cystectomy.

(2) Hemorrhage:

Types:

- 1- Intracystic.
- 2- Extracystic (intraperitoneal).

Etiology:

- 1- **Torsion:** due to severe congestion.
- 2- **Trauma:**
 - a) Direct trauma to the abdomen.
 - b) Obstetric trauma during labor.
 - c) Rough bimanual examination
- 3- **Malignancy:** due to invasion of blood vessels.

C/P:

Symptoms:

- 1- Acute abdomen.
- 2- Vomiting (peritoneal irritation).

Sign:

- 1- Signs of shock (hemorrhagic and neurogenic)
- 2- The tumor is increased in size, tense and tender (with intracystic hemorrhage).
- 3- Shifting dullness (with internal hemorrhage)
- 4- Lower abdomen is tender, rigid.

Investigations:

- 1- Ultrasonography.
- 2- Laparoscopy.

Treatment:

- 1- **Antishock measures.**
- 2- **Laparotomy:** Ovariectomy or ovarian cystectomy (If benign).
- 3- **Peritoneal toilet** (for internal hemorrhage).
- 4- **If malignant:** Treatment according to staging.

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(3) Rupture:

Etiology: The same causes of hemorrhage

Sequelae: according to the type

- 1- **Simple serous cyst:** Small amount of fluid which is not irritant is absorbed.
- 2- **Papillary serous cyst:** Persistent ascites.
- 3- **Mucinous cyst:** pseudomyxoma peritonei
- 4- **Dermoid cyst:** Chemical (aseptic) peritonitis.
- 5- **Infected cyst:** Septic peritonitis.
- 6- **Malignant cyst:** Dissimulated malignancy intra-peritoneal.

C/P:

Symptoms:

- 1- Symptomless if small and the fluid is not irritant.
- 2- Acute abdomen.
- 3- Vomiting.

Signs:

- 1- Lower abdominal rigidity and tenderness.
- 2- If unilocular cyst, it disappears.
- 3- If multilocular, the size is decreased and the shape is changed.
- 4- Shifting dullness (ascites or internal hemorrhage) may be present.
- 5- Further manifestations depend on the nature of contents.

Investigations:

- 1- Ultrasonography for intraperitoneal free fluid.
- 2- Laparoscopy.

Treatment:

- 1- Antishock measures.
- 2- Laparotomy:
 - a- Benign: ovariectomy.
 - b- Malignant: Treatment according to staging.
- 3- Peritoneal toilet.
- 4- Rubber drains; if there is infection.

(4) Infection:

- a- Spread from neighboring infected organ e.g. appendix.
- b- Ascending infection following labor or abortion.
- c- Blood-born.

C/P:

Symptoms:

- 1- Lower abdominal pain.
- 2- Pyrexia.
- 3- Vomiting.

Signs:

- 1- Rapid pulse.
- 2- Fever.
- 3- Tender, fixed tumor (adhesions)
- 4- The size may be increased.

Investigations:

- Erythrocyte sedimentation rate (E.S.R.) is increased.
- Blood picture → leukocytosis.
- Ultrasonography to diagnose a cyst.

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Treatment:

- Antibiotics + ovariectomy.
- If there are marked adhesions, marsupialization is performed (the wall of the cyst is sutured to parietal peritoneum after opening the cyst and a rubber drain is left for drainage).

(5) Incarceration in Douglas pouch:

Causes:

- 1- Adhesions.
- 2- Projecting sacral promontory.
- 3- Simple impaction.

C/P: Pelvic pain + Pressure symptoms e.g. retention of urine.

Treatment: Surgical excision.

(6) Malignant change.

NB: If malignancy is discovered after removal of apparently benign tumor, a second-look laparotomy or laparoscopy must be done or postoperative radiotherapy or chemotherapy must be given.

(7) Intestinal obstruction:

Due to adhesion resulting from infection or malignancy.

(8) Complications during pregnancy, labour and puerperium: The commonest is dermoid cyst and simple serous cyst.

- Abortion.
- Preterm labor.
- Malpresentations and non engagement.
- Pressure symptoms.
- Obstructed labor.
- Puerperal sepsis.

Management during pregnancy and labor:

1. **During first trimester:** Conservative management as the affected ovary may contain corpus luteum of pregnancy and its removal may result in abortion.
2. **During second trimester:** Removal and tocolytic drugs.
3. **During third trimester:** Conserve till delivery except if complications occur during labor.
 - If there is no obstruction for delivery, vaginal delivery is allowed with removal of the tumor very early in puerperium.
 - If the tumor causes obstruction of vaginal delivery, cesarean section is done with removal of the tumor at the same sitting.

Benign ovarian tumors

Symptoms:

Asymptomatic: Accidentally discovered.

Abdominal swelling: It is the commonest symptom.

Pressure manifestation:

- **Upper abdominal:** Dyspnea and dyspepsia "if huge tumors".
- **Pelvic pressure:** frequency of micturition "if impacted".

Pain: If complicated (torsion).

Menstrual abnormalities due to:

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- **Abnormal uterine bleeding.**
- **Feminizing ovarian tumor.**
- **Twisted tumors → marked congestion.**
- **Amenorrhea → virializing ovarian tumors.**

Ovarian cachexia: Huge mucinous tumor.

Signs:

General examination: Rarely ovarian cachexia.

Abdominal examination:

- A large tumor → pelvi-abdominal mass.
- Surface is smooth or lobulated.
- Mobile.
- Consistency is usually cystic but sometimes solid "fibroma".
- Percussion: dullness in center and resonance in flanks.
NB: Ascites causes resonance in center and dullness in flanks.

Pelvic examination: "Bimanual examination"

- Small tumors are detected by bimanual examination.
- Tumor is separate from uterus.
- Movement of tumors through abdomen is not transferred to cervix.

Differential diagnosis:

Large tumors: "Causes of abdominal swelling" [fetus, ascites, fibroid, fat (obesity), flatus and full bladder].

Small tumors: Causes of adnexal mass.

Investigations:

Imaging:

- Ultrasonography to detect ascites and ovarian mass.
- X-ray → tooth in benign cystic teratoma.
- CT and MRI are more accurate.

Endoscopy: Laparoscopy differentiates small ovarian tumor from subserous fibroid.

Tissue pathology: Biopsy and frozen section at exploratory laparotomy if malignancy is suspected.

Management:

It may be done using either laparoscopy or laparotomy.

Ovarian cystectomy:

- Removal of cyst and plication of ovarian tissue.
- Indications are young patients to preserve ovary.

Ovariectomy:

- Removal of ovary containing tumors.
- Pedicles are clamped between 2 clamps and ligated by transfixation:
 - Infundibulo-pelvic ligament.
 - Ovarian ligament and mesovarian.
- Inspection of other ovary before abdominal closure.
- Indications:
 - If ovarian tissue is damaged.
 - Complicated tumors; torsion.

NB: Oophorectomy is removal of healthy ovary.

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Total abdominal hysterectomy and bilateral salpingoophorectomy:

"Panhysterectomy" in patients > 45 years increases incidence of malignancy.

Laparoscopic surgery in benign tumors:

Patient selection:

- Simple unilocular ovarian cyst "no solid part is present".
- No doubt about benign nature (on U/S).
- CA-125 is not elevated.
- Small in size < 10 cm.
- Unilateral tumor.
- Young patient.
- Dermoid cyst is not suspected.
- Surgeon is experienced in laparoscopy.
- Patient is consented for laparotomy if needed.

Malignant tumors "ovarian cancer"

Incidence:

- It is the 3rd common malignancy of female genital tract.
- 20% of all ovarian tumors are malignant.

Risk factors:

Age: No age is immune. But maximum peak = 70 years in epithelial while \pm 30 years in germ cell tumor.

Parity: Nullipara and low parity: more exposed to trauma of ovulation.

Race: White races.

Socio-economic state: Higher social classes.

Family history: 10% of all epithelial ovarian cancers are familial.

Three familial ovarian cancer syndromes are autosomal dominant:

1- Hereditary breast-ovarian cancer syndrome.

2- Site-specific ovarian cancer syndrome:

- \uparrow number of affected relative.
- It is due to germ-line mutation in:
 - BRCA1 gene on chromosome 17.
 - BRCA2 gene on chromosome 13.

3- Lynch II syndrome (hereditary nonpolyposis colonic cancer "HNPCC").

Contraceptive pills and lactation: Protective effect.

Dysgenetic gonads: Germ cells tumors "gonadoblastoma".

Spread:

Transcoelomic spread:

- Commonest and earliest mode of spread in epithelial ovarian cancer.
- Exfoliation of malignant cells then implanted on peritoneal surfaces.
- Cells follow circulation of peritoneal fluid; Douglas Pouch, paracolic gutters, right hemidiaphragm, liver surface, intestine and finally omentum.

Direct spread:

Tube, uterus, bladder, intestine, appendix and omentum.

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Lymphatic (more common in germ cell tumors):

- Paraaortic lymph nodes, lymphatic channels through diaphragm to supraclavicular LN "Virchow's gland". Paraaortic L.N. are involved in 18% (Stage I), 20% (Stage II), 42% (Stage III), 67% (Stage IV)
- Pelvic LN along anastomosis of ovarian and uterine lymphatics and along pelvic ligaments.
- Other ovary is affected.

Blood spread: Liver, lung, bone and brain "late".

Causes of Ascites in malignant ovarian tumor:

- Obstruction of lymphatics in diaphragm "drain peritoneum" leads to peritoneal effusions.
- Oozing from surface of 1ry tumor or peritoneal implants leads to malignant ascites.
- Liver nodule leads to portal hypertension.
- Cachexia leads to hypoproteinemia.
- Hormonal stimulation or electrolytic imbalance in peritoneal fluid.

Causes of hydrothorax:

- Secondaries in lung "malignant effusion with positive malignant Cells".
- Communication between pleura and peritoneum.
- Obstruction of subphrenic lymphatics.

Staging of 1ry ovarian cancer "FIGO":

FIGO system is a surgico-pathological staging, which comprises cytological examination of Ascites or peritoneal washings.

Stage I: Growth limited to the ovaries:

- Ia: Growth limited to one ovary, capsule intact. No ascites, peritoneal wash not containing malignant cells.
- Ib: Growth limited to both ovaries. Capsule intact, no ascites, peritoneal wash not containing malignant cells.
- Ic: Tumor stage Ia or stage Ib with tumor on the surface of one or both ovaries with ascites containing malignant cells or positive peritoneal wash.

Stage II: Pelvic stage:

- IIa: Extension and/or metastases to the uterus and/or tubes.
- IIb: Extension to other pelvic tissue.
- IIc: Tumor stage IIa or stage IIb with a capsule ruptured or ascites containing malignant cell or positive peritoneal wash.

Stage III: Abdominal stage:

- IIIa: Tumor involving one or both ovaries with microscopic seedling of abdominal peritoneal surface or omentum, with negative nodes.
- IIIb: Abdominal peritoneal implants less than 2 cm. in diameter, nodes are negative.
- IIIc: Abdominal implants greater than 2 cm diameter and/or positive retroperitoneal nodes.

Stage IV: Growth involving one or both ovaries with distant metastases, parenchymal liver metastases.

Clinical picture

Symptoms:

- (1) **Asymptomatic:** It is the commonest presentation.
- (2) **Abdominal enlargement:** Rapidly growing tumor.
- (3) **Pain and vague GIT manifestation:** Dyspepsia, distension and discomfort are common.

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(4) Menstrual disturbance:

- Post-menopausal bleeding and irregular uterine bleeding:
 - Feminizing ovarian tumor.
 - Metastasis to endometrium.
 - Endometrial cancer with metastasis ovary.
- Amenorrhea:
 - Virilizing ovary tumor.
 - Ovarian tumors destructing ovarian tissue bilaterally.

(5) Cachexia.

(6) Pregnancy: *See complications.*

Signs:

(1) General examination:

- Cachexia.
- Distant spread.
- Virchow's LN.
- Unilateral L.L. edema.
- Functioning ovary tumor "virilization".

(2) Abdominal examination:

- Ascites.
- Umbilical nodule.
- Nodules in upper abdomen "liver nodule, paraaortic LN and omental cake".
- Ovarian tumor may be felt as (abdominal mass and pelvi-abdominal mass).

(3) Pelvic examination:

Ovarian tumor may be presented as:

- Mass in Douglas pouch.
- Adnexal mass.

Criteria suggesting malignancy:

- Bilaterality.
- Solidity or solid area in cystic tumor.
- Fixation.
- Tenderness.
- Nodules in Douglas Pouch.
- Ascites.
- Edema in vulva.

Early detection (screening) of cancer ovary:

- **Bimanual examination:** In postmenopausal women/ 6 month, to detect palpable ovary.
- **Ultrasonography:** Transvaginal U/S is better in early detection of ovarian tumors.
- **Colored Doppler U/S:** To detect neo-vascularization within tumors.
- **Tumor markers:** Substances secreted by tumor cells in the circulation.
- **Multimodal:** Combination of CA125 "> 35 U/ml" and ultrasonography is the best approach.

Special investigations:

(A) Imaging:

1- Ultrasonography:

Criteria suggestive of malignancy:

1. Ovarian volume > 9cm³ in post-menopausal women.
2. Bilaterality.
3. Variable echogenicity.
4. Thick septation.
5. Extracystic papillae or capsule invasion.
6. Presence of daughter cyst.
7. Presence of ascites.

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2- **Doppler velocimetry:** ↑ blood flow is evidenced by:

- ↓ S/D ratio (systolic/ Diastolic ratio).
- ↓ Resistance index (RI).

3- **CT and MRI:** To detect liver metastasis and LN involvement.

(B) **Laboratory investigations:** Tumor markers "immunodiagnosis".

N.B Tumor markers: Protein substances (hormones, enzymes or antigens) circulating in blood and body fluids denoting the presence of certain malignant tumors. They are released in the stage of transformation from benign to malignant stage i.e. early in the course of malignant tumors e.g. Cancer Antigen 125 (CA-125).

1. **Epithelial tumors:**

- **CA₁₂₅:** Cut off > 35 u/ ml for non-mucinous epithelial ovary cancer.
- **CEA and CA_{19.9}:** Mucinous epithelial ovarian cancer.

2. **Germ cell tumours:**

- **Dysgerminoma:** LDH. - **EST:** α fetoprotein.
- **Choriocarcinoma:** HCG.
- **Embryoma, embryonal carcinoma:** HCG and α FP.
- **Struma ovarii:** Thyroxin. - **Carcinoid:** Serotonin.

3. **Sex cord stroma:** *Granulosa cell tumor (estrogen-inhibin).*

(C) **Endoscopy: Laparoscopy**

- Detect small masses.
- Biopsy is taken.
- Aspiration of fluid for cytology.

Treatment of malignant tumors:

1- **Treatment of borderline tumors:**

- The principle treatment is surgical resection of 1ry tumor and follow up:
- Young patient with unilateral disease:
 - Unilateral salpingo-oophorectomy to preserve fertility.
 - The uterus and other ovary are removed after completing her family.
- Bilateral disease; total abdominal hysterectomy and bilateral salpingo-oophorectomy.
- No evidence that subsequent chemotherapy or radiotherapy will improve survival.

2- **Treatment of malignant ovarian tumors:**

A- Data suggesting malignancy on exploratory laparotomy:

- Ascites "positive cytology or hemorrhagic ascites"; Adhesions and fixation.
- Bilateral ovarian swelling.
- Consistency "solid- heterogenous".
- Douglas Pouch nodules.
- Enlarged paraaortic L.N.
- Fungation outside capsule, frozen section biopsy.
- Blood vessels on tumors surface.
- Hemorrhage in the tumor.
- Infiltration of omentum, gut and liver.

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B- Staging:

Exploration is advised in all cases when malignancy is suspected to confirm diagnosis and for staging.

- Incision: Midline or paramedian incision for adequate exposure
- Peritoneal fluid: sampling (if ascites is present) and peritoneal washing (200 ml in gutters and Douglas Pouch).
- Exploration of abdomen (right subphrenic area, liver, intestine paracolic gutter, omentum) and take multiple biopsies.
- Exploration of L.N. (Paraortic and pelvic).
- Exploration of pelvic organs "ovaries, tubes, uterus ...".
- Peritoneum and omentum:
 - Visible lesion: take a biopsy.
 - No visible lesion; multiple biopsies (Douglas Pouch, paracolic gutters and omentum).

C- Surgical techniques:

Stage I:

(A) Total abdominal hysterectomy + bilateral salpingo-oophorectomy and complete surgical staging: Plus:

- Appendectomy (a common site for metastasis).
- Omentectomy (a common site for metastasis).
- Instillation of intra peritoneal radioactive chromium phosphate or gold to treat peritoneal seeding.

(B) Fertility preservation surgery:

- Unilateral adnexectomy for young patient to preserve fertility.
- Then other ovary and uterus are removed after she completes her family.

Indications:

- Young patient to preserve fertility.
- Reliable patient for follow up.
- Stage Ia grade 1 epithelial ovarian cancer:
 - * Unilateral borderline tumor. * Unilateral germ cell tumor.
 - * Unilateral sex cord stromal tumor.

Contraindications:

- * Clear cell tumor. * Grade 3 tumor.
- * Any stage beyond stage Ia.

Stages II, III and IV:

(A) 1ry cytoreductive (Debulking) surgery:

- The principle goal is removal of all 1ry cancer and all metastatic disease if possible.
- If residual lesion < 2cm → optimal cytoreduction.
- If residual lesion > 2cm → suboptimal cytoreduction.

(B) Interval cytoreductive surgery "interval debulking surgery":

- It is performed in advanced ovarian cancer, when the primary surgery is incomplete, and residual tumor masses are left behind.
- Three courses of chemotherapy are given, followed by laparotomy to remove the residual lesions.
- Chemotherapy is then continued after the surgery.
- The survival rate at 3 years is increased by up to 20%.

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(C) Second look laparotomy or laparoscopy after initial cure.

- Is surgery performed to patient with no clinical evidence of disease after 1ry surgery and chemotherapy to detect response to treatment.
- 2nd look surgeries have been replaced by modern imaging techniques "positron emission tomography (PET-scan)" and CA125.
- Now, it has only place when there is increase in tumor marker and there is negative imaging.

If the patient can withstand surgical interference, it is advisable to operate on every case of malignant ovarian tumor provided that there is no distant metastasis

D- Chemotherapy for ovarian malignancy:

- Cancer ovary is chemosensitive.
- It should be started no longer than 8 wk after surgery.
- It is given for 6 cycles every 3 weeks.

I. Epithelial ovarian cancer:

- Low risk: Stage I_A, I_B Grade 1, 2: No-postoperative chemotherapy.
- High risk: Stage I_A, I_B Grade 3, Stage I_C, II, III, IV and Clear cell histology.

- Types:

- Platinum- based chemotherapy "**cisplatin- carboplatin**".
- The best is **combination chemotherapy; carboplatin + paclitaxel - Intraperitoneal chemotherapy**:
- It has high efficacy and low systemic side effects.
- Patient with microscopic disease is the most suitable.
- Cisplatin is the most frequently used.

II. Germ cell tumours:

- All patients should receive post-operative adjuvant therapy except: stage Ia grade I (dysgerminoma- immature teratoma).
- BEP "Bleomycin - Etoposide - Cisplatin".

III. Sex-cord stromal tumours:

Stages I_C, II, III and IV.

In the form of (carboplatin/ paclitaxel or BEP).

IV. Borderline tumours: No postoperative chemotherapy.

E- Radiotherapy for ovarian tumors:

- **External pelvic irradiation:** For radiosensitive tumors as dysgerminoma.
- **Intraperitoneal radioactive isotopes (P32 or Au198):** For ascites containing positive malignant cells or positive peritoneal washing.

F- Palliative treatment:

- **For pain:** Analgesics.
- **For cachexia:** Diet and IV hyperalimentation.
- **For ascites:** Repeated aspiration + radioisotope.

G- Immunotherapy:

- Nonspecific immunotherapy; BCG or Corynebacterium parvum with chemotherapy.
- Interferon.

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Prognosis:

It has poor prognosis due to:

- Lack of early symptoms; > 75% of patient are stage III at time of diagnosis.
- Diagnosis of pre-invasive lesion is impossible except by biopsy.
- Ovary is intra peritoneal; early spread to intestine.

Causes of death:

1. Intestinal obstruction "commonest cause of death".
2. Distant metastasis.
3. Complications are bleeding, infection and DVT.

5- year survival rate in epithelial ovarian cancer:

(1) According to age:

- < 50 years: 40%.
- > 50 years: 15%.

(2) According to stage:

- I and II: 80 - 100%.
- IIIa: 30 - 40%.
- IIIb: 20%.
- IIIc and IV: 5%.

(3) According to grade:

- Grade 1: 40%.
- Grade 2: 20%.
- Grade 3: 5- 10%.

(4) According to residual tumor:

- Microscopic residual disease: 40-75%.
- Optimal debulking (< 2 cm): 30- 40%.
- Sub-optimal debulking (> 2cm): 5%.

Para-ovarian (broad ligamentary) cyst

Etiology: Cystic dilatation of vestigial remnants of mesonephric duct between the 2 leaves of the broad ligament.

Pathological features:

- Usually unilateral.
- Unilocular, thin walled (as it is lined with flattened epithelium).
- Contains clear serous fluid.
- Pushes the uterus to the opposite side, and the tube is stretched over it.

Clinically:

Unilateral cystic mass of limited mobility is felt lateral to the uterus pushing it to the opposite side.

Investigations:

Ultrasonography: TVS or TAS.

Hysterosalpingography: The uterus is pushed to one side and the overlying fallopian tube is stretched.

Treatment: Surgical excision.

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General Remarks

Ovarian tumours occurring during childhood:

- Germ cell tumors.
- Granulosa cell tumor; Teratoma is the commonest ovarian tumor in children.

Functioning ovarian tumours (tumours producing hormones):

- Feminizing tumors → Estrogen.
- Virilizing tumors → Androgen.
- Struma ovarii → Thyroxin.
- Choriocarcinoma → HCG and H.P.L.
- Misfit tumors (originally non-functioning tumors, the stroma cells of which may produce estrogen) e.g. Brenner's tumor

Ovarian tumours causing uterine bleeding:

- Oestrogenic tumours (granulosa and theca cell tumour).
- Malignant ovarian tumour with uterine metastasis.
- Twisted ovarian tumour.
- Brenner tumour as it may secrete oestrogen.

Ovarian tumours causing amenorrhoea:

- Virilizing (androgenic) tumours. Sertoli cell tumour, Leydig cell tumour, androblastoma, gynandroblastoma.
- Cachexia from advanced ovarian malignancy
- Bilateral diffuse fibromata.

Solid ovarian tumours (20% of ovarian tumours):

- Brenner's tumour.
- 1ry solid carcinoma.
- 2ry malignant tumours of the ovary.
- All germ cell tumours except dermoid cyst.
- All sex cord stromal tumours (large tumour tend to develop cystic changes).

Malignant ovarian tumours:

- Epithelial tumours: 90%.
- Sex cord stromal tumour: 7%.
- Germ cell tumours: 3%.

N.B.

- **Dysgerminoma** is the commonest ovarian cancer occurring in pregnancy. It is very radio-sensitive, but still chemotherapy is preferred when adjuvant therapy is needed.
- **The palpable ovary syndrome:** The diameters of the postmenopausal ovary are 0.5 x 1 x 1.5 cm rendering it impalpable on bimanual examination. Any ovary palpable 3 or more years after menopause is considered pathological and indicates investigations.
- **Immunotherapy in cancer ovary:** BCG vaccine increases response of immune system to tumor.

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Vulval Ulcers

Traumatic:

- Defloration injury.
- Infected perineal tear or episiotomy.

Inflammatory:

(I) Sexually transmitted:

A. Syphilitic ulcers: caused by *treponema pallidum*.

- Chancre: painless, rounded, punched out edge, red floor, indurated base and inguinal L.N firm, mobile, not tender, does not suppurate.
- Break down of mucous patch or condylomata lata.
- Ulcerating gumma: surrounded by edema and induration.

B. Chancroid (soft sore): caused by *haemophilus ducreyi*.

- Painful soft ulcer and inguinal L.N are painful and suppurate.
- Gram stain and culture: gram negative bacilli.
- Treatment: erythromycin and tetracycline.

C. Lymphogranuloma venereum: caused by *chlamydia trachomatis* L₁, L₂, L₃.

- Small ulcer appear on perineum and disappear rapidly.
- Inguinal L.N: are matted together → break down into multiple abscess discharging pus.
- It leads to chronic lymphatic obstruction → vulval elephantiasis + rectal stricture and fistula are common.
- Investigations: like chlamydial genital infections.
- Treatment: tetracycline or erythromycin → 21 days.

D. Granuloma inguinal: caused by *calymatobacterium granulomatis* or Donovan bodies.

- Papule or vesicle → ulcerate.
- Inguinal L.N. → do not suppurate.
- Investigation: encapsulated gram negative organism inside mononuclear cells (Donovan bodies).
- Treatment: Erythromycin or tetracycline.

E. Herpes simplex ulcers: Multiple small vesicles → multiple small shallow ulcers → painful.

(II) Non-sexually transmitted:

A. Tuberculus: single or multiple, serpiginous outline, undermined edge, soft base, yellow floor.

B. Bilharziasis: single or multiple with sharp edge, granular floor, firm base.

C. Diphtheritic ulcer: in children → covered by grayish membrane that bleeds on removal.

D. Crohn's disease: knife like cuts.

Neoplastic:

- Rodent ulcer (basal cell carcinoma):

- Beaded rolled in edge.
- Indurated base. It is locally malignant tumor.

Treatment: surgical excision with wide safety margin.

- Carcinoma:

Raised everted edge, necrotic floor, indurated base and inguinal L.N → indurated and enlarged.

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Aphthous ulcer:

- Painful shallow ulcer with yellow base and red margin.
- It may be cyclic (appear pre-menstrual and healing during or after menstruation without scarring)
- like the mouth.

Behcet syndrome: "autoimmune disease"

- Oro-genital ulcers, iridocyclitis, joint pains, skin nodules.
- Treatment by corticosteroids.

Vulval Swellings

I. Swellings arising from vulva "true vulval swellings":

(1) Congenital:

- Hypertrophy of the clitoris.
- Hypertrophy of labia minora.
- Congenital dermoid cyst: at mid-line.
- Clitoridal or hymeneal cyst: arise from the lower end of Gartner's duct in mid-line anteriorly.

(2) Traumatic: Haematoma

Etiology:

- Direct trauma. - Surgical trauma (excision of Bartholin's cyst).
- Obstetric trauma.

Treatment:

- Small → wait for spontaneous absorption and give antibiotic.
- Large or ↑ in size → incision, ligation of bleeding vessel.

(3) Vascular causes:

- **Varicose vein:** tortuous dark blue soft structure that become prominent on standing and empty on lying down common in pregnancy.
- **Odem:**
 - Congestive H.F. and renal disease. - Vulvitis.
 - Pelvic tumors. - Pre-eclampsia and obstructed labor.
- **Elephantiasis:** chronic lymphatic obstruction (congenital - acquired "W. bancrofti- T.B.- LGV."

(4) Inflammatory:

- Acute vulvitis.
- Bartholinitis and Bartholin's abscess.
- Hypertrophic T.B.
- Bilharzial polyps "pseudo-elephantiasis".
- Condylomata lata.
- Condylomata acuminata.

(5) Neoplastic:

(A) Benign:

- Papilloma, adenoma of Bartholin's gland, hidradenoma (adenoma of sweat gland).
- Fibroma, lipoma, hemangioma.

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(B) Malignant:

- 1ry tumors: vulval carcinoma, sarcoma, melanoma.
- 2ry tumors: spread from uterus, vagina.

(6) Retention cysts:

A- Bartholine cyst: it is the commonest cyst of vulva.

Etiology: Occlusion of duct by Fibrosis following trauma (mediolateral episiotomy, cycling) or infection (bartholinitis) or inspissated thick mucous or epithelial cells.

Pathology:

- Cyst of duct: more common lined by transitional epithelium
- Cyst of gland: less common lined by columnar epithelium

Complication:

- Infection → bartholinitis and bartholine abscess by Gonoc

C/P: Swelling in the posterior part of labia majora.

- Painless, unless infected.
- Cause dyspareunia: if large or infected.
- Bartholine abscess: swelling in posterior part of labia majora which is tender, hot, red.

Treatment:

- Bartholin cyst:
 - A) Marsupialization: The cyst is incised and edges are sutured to the skin.
 - B) Excision:- in post menopausal women to excluded cancer.
- If recurrent.



Advantage of marsupialization over excision:

- 1- Easy with less bleeding.
 - 2- Preserve the function of gland.
 - 3- Shorter healing time.
- Bartholinitis: Antibiotics + hot fomentation + rest.
 - Bartholine abscess: incision and drainage outside vaginal introitus.

B- Sebaceous cyst:

- Small cysts. - Usually multiple.
- Caused by retention of sebum by occlusion of duct.

C- Inclusion dermoid cyst:

- Small cyst containing sebaceous material resulting from implantation of epithelial cells of skin below surface epithelium, secreting sebaceous material → forming a cyst.
- This occur at time of repair of episiotomy, perineal tears, posterior colpoperineorraphy, circumcision.
- It occurs in: clitoris, posterior vaginal wall, perineum.
- Treatment: surgical excision.

D- Endometrioma: small dark bluish cyst which ↑ in size during menstruation. It is lined by endometrium and contain altered blood.

E- Hydrocele of canal of Nuck:

- Canal of Nuck: is a pouch of peritoneum passing in inguinal canal during development which is normally obliterated.
- Hydrocele of canal of Nuck is unobliterated canal of Nuck containing fluid.
- Clinically:
 - * It forms a cyst in upper part of labia majora.

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- Hernia of canal of Nuck: remains communicating with peritoneal cavity → evacuate on lying down.
- Treatment: surgical excision of sac.

II. Swellings appearing at vulva:

- (1) Vaginal swellings: (Prolapse- tumors) See D.D. of prolapse.
- (2) Uterine swellings and cervical swellings: See D.D. of prolapse.
- (3) Inguinal swellings:
 - Inguinal hernia (reducible- impulse on cough).
 - Hydrocele of canal of Nuck.
 - Swellings of Round lig. "endometriosis".
 - Testis: in testicular feminization.
- (4) Urethral swellings:
 - Urethral caruncle.
 - Urethral diverticulum.
 - Urethral prolapse.
 - Urethral tumors.
 - Skene's tubules cyst.

Causes of vulvar cysts:

- 1- Clitoridial, hymenal cyst.
- 2- Congenital dermoid cyst.
- 3- Haematoma.
- 4- Retention cysts.
- 5- Bartholin's cyst and abscess.

Urethral caruncle:

It is a small red pedunculated mass arising from the floor of the urethra and protrudes from the external urethral meatus.

- Pathology:

- Usually single.
- It consists of:
 - Covering epithelium: transitional epithelium.
 - Granulation tissue infiltrated by lymphocytes.
 - Blood vessels.
- It has 3 types:
 1. Papillomatous caruncle (true caruncle) → papilloma of urethra.
 2. Granulomatous caruncle: mainly granulation tissue due to chronic urethritis.
 3. Angiomatous caruncle: contains dilated blood vessels.
- Symptoms: pain, dysuria, dyspareunia, bleeding or presence of swelling.
- D.D.:
 - Urethral carcinoma.
 - Prolapsed urethral mucosa.
- Treatment: wide surgical excision + cauterization of the base.

Prolapse of urethral mucous membrane:

- (1) Acute type:
 - In pre-menarcheal or post-menopausal women (↓ E).

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- It appears after coughing, crying and sever straining.
- It forms purple swelling of variable size with the urethral meatus at its center.
- C/P: pain, dysuria, urine retention.
- Treatment:

1. Surgical excision of redundant mucosa.
2. Simple ligation over a catheter → sloughing.
3. Manual reduction.

(2) Chronic type:

- It occurs in old age → external meatus gape and allow some part of urethral mucosa to project as small tumor.
- It is usually asymptomatic unless infected → dysuria, frequency.
- Treatment:
 - * No symptoms = no treatment.
 - * If symptomatizing → excision of redundant mucosa.

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Vulval intra-epithelial neoplasia

Definition:

It is malignant change in epithelial covering of vulva without invasion of Basement membrane.

Classification:

- (1) VIN I (mild dysplasia): the lower 1/3 of epithelium is replaced by abnormal cells. Recently has been eliminated from classification.
- (2) VIN II (moderate dysplasia): the lower 2/3 of epithelium is replaced by abnormal cells.
- (3) VIN III:
 - **Sever dysplasia:** > the lower 2/3 of epithelium is replaced by abnormal cells.
 - **Carcinoma in situ** (carcinoma simplex): the whole thickness of epithelium is replaced by abnormal cells + no invasion of B.M.

Abnormal cells:

- **Nuclear atypia:** large, irregular in size, hyperchromatic, dense chromatin clumping, large nucleoli, abnormal mitotic figures.
- **Nucleo-cytoplasmic ratio** is increased.
- **Loss of stratification of cells.**

Specific types of VIN:

Bowen's disease: Intra-epithelial neoplasia characterized by presence of Bowen's cells (large multinucleated cells + cytoplasmic vaculation around nuclei).

Paget's disease: characterized by presence of large rounded or oval cells + large central hyperchromatic nuclei + vacuolated cytoplasm due to presence of mucin.

- Paget's cells are found near basal layer of epithelium.
- About 25% are associated with underlying carcinoma of sweat gland.
- Clinically: sharply demarcated hyperemic area. It may be covered by white areas "cake icing" → pathognomonic for Paget's.
- **Treatment:** wide local excision + exclude underlying adenocarcinoma.

Diagnosis of VIN:

Age: average age is 35-40y (30- 40y earlier than invasion).

Symptoms: asymptomatic > 50% - pruritis vulvae.

Signs:

- No visible lesion.
- Bright or dark red or white patches.
- It is usually multifocal "several areas of vulva" and may affect perineal skin, vagina, cervix. So, the whole genital tract is examined carefully.

Investigations:

1. **Colposcopy:** show white lesions and areas of abnormal vascularity.
2. **Toluidine blue test (Collin's test):** toluidine blue 1% applied to vulva and left for 3 minutes, then washed with 1% acetic acid → Abnormal areas remain blue.
3. **Tetracyclin fluorescence:** it delineates areas with high metabolic activity.
4. **Biopsy:** taken from suspected area. It is the only definitive diagnosis.

Treatment:

- **Local excision:** with generous margin of healthy tissues (0.5- 1cm).

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- Simple vulvectomy: extensive lesion and patient > 50y.
- Skinning vulvectomy: removal of vulval skin without s.c. tissue, followed by covering vulva with skin graft. Done in young patient with extensive lesion. To avoid complication of vulvectomy (disfigurement, dyspareunia, ↓ sexual arousal, loss of libido, psychological disturbance).
- LASER ablation or excision.
- Topical 5% 5-fluoro-uracil ointment: (5fu) → cytotoxic that inhibits DNA and RNA synthesis.

Recurrence: 30-50% → follow up is mandatory.

Invasive vulval carcinoma

Definition:

Malignant change of epithelium covering vulva with invasion of basement membrane.

Incidence: 4th common invasive malignancy of ♀ genital tract (4%).

Risk factors:

- Age: 60- 70 years.
- Prolonged vulval irritation: (chemical- mechanical- infective “\$, LGV, GI, HPV: 16 - 18”).
- Immunodeficiency: AIDS and patients of organ transplantation.
- Smoking.
- DM “in 10%”, obesity and HPN “30- 50%” some endocrinopathies.

Pre-cancerous lesions:

Vulval intra-epithelial neoplasia (VIN):

- VIN II (moderate dysplasia)
- VIN III (severe dysplasia and carcinoma insitu)

Human papilloma virus infection: high risk types 16, 18.

Vulval dystrophy “hyperplastic and mixed types with atypia”:

Present in more than 50% of cases.

Pathology

Sites:

Commonest sites are (labia majora → clitoris → L. minora). It may be multifocal. Kissing ulcer “due to lymphatic spread, direct contact, multifocal diseases”.

Macroscopic picture:

- Cauliflower mass.
- Malignant ulcer: raised everted edge, necrotic floor and indurated base.
- Nodular lesion.

Microscopic picture:

- Squamous cell carcinoma (90%).
- Basal cell carcinoma.
- Adenocarcinoma (1-2%) of Bartholin's gland.
- Malignant melanoma (8-10%).

Spread:

Direct spread: urethra, bladder- vagina, perineum, anus, groin.

Lymphatic spread:

- Early.

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- To lymphatics of both sides.

Iry relay: - superficial inguinal L.N. - Superficial femoral L.N.

Intermediate relay: Deep inguinal L.N. Deep femoral L.N. (L.N. of cloquet).

Deep relay:

External iliac L.N.

Common iliac L.N.

Para aortic L.N.

- Tumors of clitoris and bartholine gland spread directly to intermediate or deep group.

Blood spread: Late to liver, lung, bone, brain.

In case of melanoma → it occurs early.

Implantation: "Kissing ulcer" → doubted.

FIGO staging of vulval carcinoma 2009:

Stage I: Tumor confined to vulva and perineum.

IA: lesions ≤2cm in diameter and stromal invasion ≤1mm - no L.N. metastasis.

IB: lesions >2 cm in diameter and/or stromal invasion >1 mm - no L.N. metastasis.

Stage II: Tumor of any size with extension to adjacent perineal structure (lower 1/3 of urethra, lower 1/3 of vagina and anus) - no L.N. metastasis.

Stage III: Tumor of any size with or without extension to adjacent perineal structure + positive inguino-femoral L.N. metastasis

IA: one L.N. > 5mm or 1-2 L.N. < 5mm

IB: 2 or more L.N. > 5mm or 3 or more L.N. < 5mm

IC: positive L.N. with extra capsular spread.

Stage IV:

IVA Tumor invade any of the following:

A1 Upper 2/3 of urethra, bladder mucosa, upper 2/3 of vagina, rectal mucosa or pelvic bone.

A2 Fixed or ulcerated inguino-femoral L.N.

IVB Any distant spread including pelvic L.N.

Complications:

- Cachexia.
- Infection.
- Hemorrhage
- Spread.
- Thrombophlebitis + pulmonary embolism
- Complication of treatment: Vulvectomy
- Commonest cause of death is *hemorrhage*.

Clinical picture:

Symptoms:

Pruritus vulvae "earliest symptom", Postmenopausal bleeding, swelling, serosanguinous discharge, Soreness of vulva, Asymptomatic (in 20%)

Signs:

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- **General:** Cachexia and distant spread
- **Abdominal:** liver for metastasis
- **Local:** cauliflower mass, ulcer, nodular mass

Investigations:

- **For screening:** Cytology "scraping", Colposcopy and Toluidine blue dye "Collin's test"
- **Confirm diagnosis:** Biopsy
- **To certify spread:** metastatic work up
- **Preoperative preparation:** CBC, Blood sugar, Liver function, Kidney function, Urine analysis, ECG

Differential Diagnosis: for causes of pruritis vulva, post-menopausal bleeding, Vulval swelling, Vulval ulcers

Treatment:

- 1) Prophylaxis: avoid risk factors, proper treatment of risk factors, screening for vin, proper treatment and follow up of vin

- 2) Active treatment:

Plan of management:

- **Stage I, II:** Modified radical vulvectomy + inguino-femoral lymphadenectomy.
- **Stage III, IV:** according to general condition → Radical or extensive surgery (+/- Radiotherapy).
- **Modified Radical Vulvectomy:**
 - The original butterfly incision to remove vulva, inguinal and femoral L.N is now replaced by smaller triple incisions. ± Pelvic irradiation if pelvic L.N are involved or L.N of cloquet.
- * **Stage IA "micro invasive carcinoma"** < 1mm in stromal invasion → Wide local excision (3 cm safety region) + no lymphadenectomy. Aiming to decrease postoperative morbidity.
- **Radiotherapy:**
 - Patient unfit for surgery.
 - Refuses surgery
 - Recurrent tumor.
 - Post-operative



Prognosis (5 years survival rate):

- **Stage I:** 90%.
- **Stage II:** 80%
- **Stage III:** 50%.
- **Stage IV:** 20 %

Verrucous carcinoma

It is papillary squamous cell carcinoma, can occur at vulva, vagina and cervix. It resembles condylomata acuminata. Spread to L.N doesn't occur. It is treated by wide local excision or simple vulvectomy. Radiotherapy is **contraindicated** (anaplastic change and rapid spread)

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Non-neoplastic vulval epithelial disorders

As the term dystrophy means deficient nutrition, the international society for the study of vulval diseases (ISSVD) has developed the term "non-neoplastic vulval epithelial disorders".

The ISSVD classification:

- *Lichen sclerosus et atrophicus* (old name hypoplastic dystrophy).
- *Squamous cell hyperplasia* (old name hyperplastic dystrophy).
- *Other dermatoses*: a. Inflammatory. b. Bullous. c. Ulcerative.

Etiology:

- Chronic mechanical skin irritation .
- Local decrease in 5-alpha reductase, DHT .
- Autoimmune disorders e.g. Achlorhydria .
- Nutritional deficiency .
- Others; DM, chalcones, HSV infection.

Pathology:

Lesions are characterized by hyperkeratosis + either thickening or thinning of *epithelium* + chronic inflammatory reaction in connective tissue.

1- Lichen sclerosus:

- Occurs in early menopausal years.
- It is the most common white lesion of the vulva.
- Malignant potential is 0-9 %.

Grossly, the skin appears thin and wrinkled (parchment -like) and in advanced stages, there is loss of subcutaneous fat leading to flattening of the labia and narrowing of the vaginal introitus.

Microscopically:

- Hyperkeratosis.
- Atrophy of all layers of the epidermis .
- 3. Flat rete pegs.
- Subepithelial inflammatory cell infiltration .

2- Squamous cell hyperplasia:

- Occurs in premenopausal women
- Malignant potential is 5%
- Grossly, the lesion appears as raised whitish area and sometimes pinkish with small fissures due to scratching.

- Microscopically:

- Hyperkeratosis.
- Hyperplasia of all epidermal layers (basal cell hyperplasia, acanthosis, parakeratosis).
- Deep rete pegs.
- Subepithelial inflammatory cell infiltration.

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Diagnosis:

Symptoms:

- Asymptomatic.
- Pruritus vulvae (scratch, itch, scratch cycle).
- Superficial dyspareunia.
- Vaginal discharge may be associated.

Signs: The gross picture of the lesion is evident.

Investigations:

- Toluidene blue directed biopsy.
- Colposcopy and colposcopically directed biopsy.
- Investigating predisposing factors as DM and HSV.

Differential diagnosis of white lesion:

Non-neoplastic vulval epithelial disorders, VIN, Paget disease, cancer vulva, condyloma, vitiligo, candida and psoriasis.

Treatment:

- 1- General measures (avoid scented baths, wear white cotton under clothes and use aqueous creams for cleaning).
- 2- Treatment of predisposing factors.
- 3- Specific treatment of lichen sclerosus:
 - ERT in postmenopausal cases.
 - **Clobetasol (0.05%):** Ultrapotent corticosteroid which is very effective in controlling resistant lesions within 3 months.
 - **Oral retinoids:** 65% success rate but causes skin dryness and is teratogenic in young cases needing fertility.
 - **Local testosterone 2% cream** (not used).
 - **Photodynamic therapy.**
 - **Surgery** (perineoplasty for introital stenosis, release of clitoral adhesions).
- 4- Specific treatment of squamous cell hyperplasia:
 - Local corticosteroid e.g. Hydrocortisone 1% cream for 6 weeks.
 - Surgery if there is atypia (skinning vulvectomy).

Other dermatoses:

Inflammatory.

Bullous.

Ulcerative lesions of the vulva.

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Pruritus vulvae

Etiology:

General:

- **Systemic diseases:**
 - Diabetes mellitus.
 - Jaundice (increased bile salts).
 - Uremia (increased plasma histamine).
 - Leukemia.
 - Hypothyroidism (dry skin).
 - Allergy.
 - Achlorhydria(autoimmune).
 - Menopause.
 - Psychologic.
- **Local condition:**
 - Non neoplastic vulval epithelial disorders.
 - VIN.
 - Cancer vulva.
 - Acute vulvitis (bacterial, fungal or parasitic).
 - Secondary to anal pruritus (oxyuris infestation).
 - Coitus interruptus.
 - Idiopathic.
 - Pruritus secondary to irritant vaginal discharge.

Examination:

- General and abdominal: For evidence of DM, jaundice, thyroid diseases.
- Local: To detect vulvitis or VIN, etc.....

Investigations:

- Fasting blood sugar.
- Vulval scraping examination for fungal infection.
- Full blood examination, serum bilirubin, T3, T4 and RFT.
- Biopsy from suspicious lesions.
- Sensitivity tests.

Treatment:

Treatment of the cause.

General: sedatives and antihistaminics.

Local:

- Local cleanliness.
- Antipruritic lotions (calamine, hydrocortisone).
- Local estrogen in postmenopausal women.

Resistant cases:

- Subcutaneous infiltration with local anesthetic or corticosteroid.
- Subcutaneous 95% alcohol.
- Circular incision to cut nerve fibers or rarely simple vulvectomy.

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Vaginal swellings

I- Swellings arising from vagina:

A) Cystic swellings:

1- Gartner cyst:

- It arises from Gartner duct (wolffian system remnant).
- It arises in antero-lateral wall of vagina.
- It is the 2nd commonest cyst in vagina.
- Treatment: excision or marsupialization.

2- Implantation dermoid cyst: "commonest cyst of vagina"

- It results from implantation of skin under surface epithelium during repair of episiotomy or perineorrhaphy.
- It is lined by stratified squamous epithelium and contains sebaceous material.

3- Mullerian cyst: multiple small cysts arise from remnants of Mullerian duct.

4- Haematoma: traumatic or ruptured varicose vein.

5- Emphysema:

- Bullae filled with gas, during pregnancy due to infection with *T.vaginalis* or *Gardenerella vaginalis*.
- It causes excessive vaginal discharge.

6- Endometriotic cyst (in rectovaginal septum).

B) Solid vaginal swellings:

1- Benign neoplasm:

Papilloma, adenoma, fibroma, lipoma, angioma.

- C/P: Small: Asymptomatic

Large: Dysparunia, discharge, bladder and rectal irritation and obstructed labor.

- Treatment: Excision especially if symptomatic

2- Malignant neoplasm:

(A) 1ry:

- 1- Squamous cell carcinoma.
- 2- Adenocarcinoma.
- 3- Malignant melanoma.
- 4- Lymphoma.
- 5- Sarcoma: Adult: spindle cell sarcoma.
Children: sarcoma botryoids.

(B) 2ry: "more common than 1ry"

- 1- Direct spread from: Cervical, vulval, rectal, U.B. and urethral tumors.
- 2- Retrograde lymphatic spread from: choriocarcinoma, ovarian, renal and uterine.
- 3- Blood spread through Azygos or retrograde vascular spread: endometrial carcinoma and choriocarcinoma.
- 4- Seeding: cells of endometrial carcinoma are implanted in vaginal vault after hysterectomy.

3- Granuloma: Following total abdominal hysterectomy.

4- Inflammatory: Condylomata acuminata. Bilharzial papillomata.

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5- Vaginal adenosis: In women exposed to DES in utero.

II Swellings appearing in the vagina:

- 1- Cervical swellings → see D.D. of prolapse.
- 2- Uterine swellings → see D.D. of prolapse.
- 3- Urethral swellings → see D.D. of prolapse.

Premalignant lesions of vagina

Vaginal adenosis:

- Presence of cervical glands in the vagina due to exposure to DES in utero.
- It may progress to clear cell carcinoma.
- Follow up by cytology and colposcopy is required.

Vaginal intra epithelial neoplasia: VAIN

Definition:

Malignant change in epithelial lining of vagina without invasion of basement membrane. It may be associated with similar lesions in Cervix. and vulva

Grades:

VAIN I: Mild dysplasia: atypical cell in lower 1/3 of epithelium

VAIN II: Moderate dysplasia: atypical cell in lower 2/3 of epithelium

VAIN III: Severe dysplasia: atypical cell in upper 2/3 of epithelium

Carcinoma insitu: the whole thickness is replaced by malignant cells and no invasion of BM

Diagnosis:

- Usually asymptomatic.
- Cytology.
- Colposcopy and biopsy.
- Schiller iodine test.

Treatment:

- Wide local excision for uniform accessible lesion.
- CO2 laser: vaporization of lesion
- Total or partial vaginectomy
- Vault radiotherapy to preserve sexual function.

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Vaginal carcinoma

Definition:

Malignant changes of epithelial lining of the vagina with invasion of basement membrane.

Incidence: 5th common invasive malignancy of female genital tract (2%).

Etiology: Unknown.

Risk factors:

- Age: 60-80 years.
- Chronic vaginal irritation.
- Human papilloma virus infection.

Pre-cancerous lesions:

- VAIN (Vaginal intraepithelial neoplasia).
- Vaginal adenosis (adenocarcinoma).

Pathology:

- Site: upper 1/3 of posterior wall (commonest) or lower part of anterior vaginal wall (2nd commonest).
- MAC:
 - Cauliflower mass.
 - Ulcerative lesion.
 - Diffuse infiltration.
- MIC: **Squamous cell carcinoma (90%)**, Adenocarcinoma (on top of vaginal adenosis) or Sarcoma (sarcoma botryoids in young girls)

Spread:

- (1) Direct spread: to bladder, urethra, rectum, cervix, vulva.
- (2) Lymphatic spread:
 - Upper 1/3: like cancer Cervix.
 - Middle 1/3: internal iliac L.N
 - Lower 1/3: like cancer vulva.
- (3) Blood spread: Distant spread to lung, liver, bone and brain

FIGO Staging:

Stage 0: intraepithelial carcinoma.

Stage I: Limited to vagina.

Stage II: Extension to paravaginal tissue not reach lateral pelvic wall.

Stage III: Extension to lateral pelvic wall.

Stage IV: (A) Bladder and rectal mucosa and pelvic bone and bil L.N.

(B) Distant metastasis.

"If the tumor is involving cervix it is classified as cancer cervix and if it is involving the vulva it is classified as cancer vulva".

Complications:

- General: infection, hemorrhage, spread, cachexia.
- Specific: uremia, fistula (Bladder - Rectum).
- Commonest cause of death: uremia or hemorrhage.

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Clinical picture:

Symptoms:

- 1- May be Asymptomatic
- 2- Vaginal discharge: offensive, blood stained.
- 3- Irregular or contact vaginal bleeding.
- 4- Vaginal mass.
- 5- Dyspareunia.
- 6- Symptoms of spread: Dysuria, dyschesia and Incontinence.
- 7- Cachexia.

Signs:

- 1- **General examination:** cachexia, HPN, distant spread.
- 2- **Abdominal examination:** palpate liver for metastasis.
- 3- **Local examination:** cauliflower (friable, necrotic, bleeds on touch), ulcerative or infiltrative.

N.B.: To diagnose as 1ry vaginal cancer: Cervix and vulva shouldn't be involved

Investigations:

- (1) **Screening:**
 - Cytology.
 - Colposcopy.
- (2) **Confirm diagnosis:** Biopsy
- (3) **Certify spread:** metastatic work-up.
- (4) **Pre-operative preparation.**

Differential Diagnosis:

Causes of vaginal discharge, postmenopausal bleeding, vaginal ulcers and swellings.

Treatment:

(1) Prophylactic treatment:

- 1- Avoid risk factors.
- 2- Proper treatment of risk factors.
- 3- Screening of VAIN.
- 4- Proper treatment and follow up of VAIN.

(2) Active treatment:

- **Radiotherapy:** Treatment of choice
 - 1- External irradiation: "Deep X-ray or super voltage therapy 5000-6000 R"
 - 2- Internal irradiation: radium or cesium special applicator.
- **Surgery:**
 - 1- Tumor of upper 2/3: Radical hysterectomy and partial or total vaginectomy
 - 2- Tumors of lower 1/3: radical vulvectomy and lower vaginectomy.
 - 3- Advanced cases involving Rectum and Bladder → pelvic exenteration.
- **Recurrent cases:** Palliative.

Prognosis: Generally poor as vaginal wall is thin and rich in lymphatics and blood.

VIII. Miscellaneous topics

Miscellaneous topics Chronic pelvic pain

Definition: Pain lasting more than 6 months.

Innervation of pelvic organs:

- Pain from the perineum, vulva and lower vagina is transmitted via the pudendal nerves (S2, S3, S4).
- Pain from the upper vagina, cervix, uterus, fallopian tubes and ovaries is transmitted by autonomic nerves (T10, T11, T12 and L).

Etiology:

I. Gynecological Causes:

A. Cyclic Pain:

- Primary and secondary dysmenorrhea.
- Ovulation (Mittelschmerz) pain.
- Adenomyosis.
- Hematocolpos.
- Pelvic congestion or pelvic pain syndrome.

B. Acyclic Pain

- Chronic PID.
- Endometriosis.
- Ovarian masses.
- Uterine neoplasms or uterine prolapse.
- Intrauterine contraceptive device.
- Pelvic adhesions.

II. Non-gynecological Causes:

- **Urinary:** e.g. Urethritis, cystitis etc.
- **Intestinal:** e.g. Crohn's disease, ulcerative colitis etc.
- **Musculoskeletal.**
- **Systemic Diseases:** e.g. S.L.E.

III. Psychogenic Pelvic Pain:

Diagnosed by exclusion of other causes.

IV. Idiopathic Pain.

Diagnosis of chronic pelvic pain:

History:

- Characteristics of pain:
 - Onset, course and duration.
 - Character.
 - Site, extent and relation to menstruation.
 - Associated symptoms.
- Menstrual, obstetric, past and sexual history.
- Gastrointestinal and urinary symptoms.

VIII. Miscellaneous topics

Physical Examination:

It includes general, abdominal, pelvic and rectal examinations.

Investigations:

- Laboratory tests. C.B.C. and E.S.R.
- Ultrasound.
- CT scan and MRI.
- X-Ray examination: - I.V.P.
- Barium enema.
- Laparoscopy. Indicated for patients with unexplained chronic pelvic pain.

Treatment:

- Treatment of the cause.
- Psychotherapy.

Gynecologic causes of acute abdomen

Ovarian causes: complication in an ovarian cyst (ruptured corpus luteum cyst).

Tubal causes: Acute salpingo-oophoritis. ruptured ectopic pregnancy.

Red degeneration of a fibroid.

Pelvic peritonitis due to any cause and ruptured tubo-ovarian abscess.

Perforation of the uterus during insertion of an IUCD.

Pelvi-abdominal swelling

I. Uterine Causes:

- Normal Pregnancy:
 - The commonest cause of pelvi-abdominal swelling in the childbearing period.
 - There are symptoms and signs of pregnancy.
 - For diagnosis of pregnancy: (see obstetrics).
- Abnormal Pregnancy: e.g. vesicular mole and polyhydramnios.
- Fibroids: The patient is usually above 35 years and nullipara.
- Large Hematometra:
 - It is due to cervical stenosis which may be congenital or acquired.
 - There is amenorrhea and abdominal pain.
 - The uterus is symmetrically enlarged and the uterine sound can't be passed through the stenosed cervix.
- Large Pyometra.

II. Tubal Causes:

- In rare cases, a hydrosalpinx or pyosalpinx is felt above the inguinal ligament.
- It is usually bilateral and tender.

III. Ovarian Tumors:

- The patient is of any age and parity.
- Pain is absent unless there is a complication as torsion or malignancy.
- It should be differentiated from fibroid. (see ovarian tumors)

IV. Broad ligamentary causes:

- Broad Ligament Cyst: It is felt to one side of the uterus and pushing it to the opposite side.
- Broad Ligament Hematoma:
 - There is a history of the cause e.g. rupture of tubal pregnancy, incomplete rupture of the uterus, or incomplete hemostasis after pelvic operation.
 - It is associated with signs of internal hemorrhage.
- Broad ligamentary fibroid.

VIII. Miscellaneous topics

V. Acute Parametritis

Mass in Douglas Pouch:

I. Uterine:

- Retroverted uterus → the commonest cause.
- Posterior wall fibroid.

II. Tubal:

- Hydrosalpinx or pyosalpinx.
- Tubal ectopic pregnancy.
- Tubal neoplasm.

III. Ovarian:

- Ovarian mass.
- Prolapsed ovary.

IV. Pelvic Hematocoele:

- History suggestive of disturbed ectopic pregnancy in the form of recurrent attacks of lower abdominal pain, fainting and vaginal bleeding after a period of amenorrhea.
- Pressure symptoms in the form of dysuria I dyschezia and dyspareunia.
- Pelvi-abdominal mass which is fixed I tender and ill-defined. The uterus is pushed forwards.
- Blood on aspiration of Douglas pouch.

V. Pelvic Abscess:

- History of pelvic infection or surgery.
- There is fever, malaise, pelvic pain, dyspareunia, dysuria and dyschezia.
- Aspiration of Douglas pouch reveals pus.

VI. Hematocolpos:

- Due to imperforate hymen or transverse vaginal septum.

VII. Advanced extrauterine pregnancy.

VIII. Pelvic Kidney.

IX. Retroperitoneal Tumor.

X. Mass in The Rectum:

- Fecal mass.
- Cancer rectum.

XI. Endometriosis of the rectovaginal septum

Pelvi-abdominal swelling associated with abnormal bleeding

I. Complications of pregnancy:

- Abortion, vesicular mole, ectopic pregnancy associated with a large pelvic hematocoele.
- Antepartum hemorrhage, postpartum hemorrhage.
- Broad ligament hematoma due to cervical lacerations during labor.

II. Uterine causes:

- Fibroids.
- Uterine sarcoma.

III. Ovarian causes:

- Malignant, and estrogenic ovarian tumors.

VIII. *Miscellaneous topics*

IV. **Large hydro or pyosalpinx** (menorrhagia due to pelvic congestion)

Pelvi-abdominal swellings associated with amenorrhea

- Pregnancy.
- Encysted tuberculous peritonitis.
- Androgenic ovarian tumors.
- cases of cryptomenorrhea causing large hematocolpos or hematometra.

Symmetrical enlargement of the uterus

- Pregnancy
- Ectopic pregnancy.
- Sub-involution of the uterus
- Metropathia hemorrhagica
- Submucous or single interstitial fibroid
- Diffuse adenomyosis
- Hematometra
- Pyometra
- Early malignant tumor as carcinoma.

Mass protruding from the cervix

- Cervical polyp of any type.
- A polyp arising from the uterine body.
- The inverted uterus.
- Inevitable and incomplete abortion.

Contact bleeding

Definition:

It is bleeding occurring after intercourse, vaginal examination or douching

Causes:

I. Cervical:

- Carcinoma of the cervix.
- Cervical erosion (ectopy).
- Ulcers of the cervix.
- Cervical polypi.

II. Vaginal:

- Vaginal carcinoma
- Granulation tissue in the vaginal vault after total hysterectomy.

Adnexal mass

- **Ovary:** Functional cyst, neoplasm. endometriosis and ovarian pregnancy
- **Tube:** Hydrosalpinx. pyosalpinx, tubal pregnancy and neoplasm
- **Broad ligament:** Para ovarian cyst and broad ligament fibroid.
- **Uterus:** pedunculated subserous fibroid.
- **Bowel:** Appendicitis, diverticulitis and colonic cancer.
- **Miscellaneous,** e.g. Distended bladder.

VIII. Miscellaneous topics

Hormones In Gynecology

| | Estrogen | Progesterone |
|--------------------------------|--|---|
| Types | <p>(1) Types of estrogens produced in females :</p> <ul style="list-style-type: none"> - E1 (estrone): mainly produced by peripheral conversion of androstenedione. - E2 (estradiol) secreted from the ovary. - E3 (estriol): the metabolite of E1 and E2]. <p>(2) Natural forms:</p> <ul style="list-style-type: none"> - conjugated equine estrogens (Premarin) - Piperazine estrone sulphate. - Estradiol 17-B. <p>(3) Synthetic forms:</p> <ul style="list-style-type: none"> - Ethinyl estradiol - Mestranol. | <p>(1) Natural progestagen Progesterone.</p> <p>(2) Synthetic progestagen:</p> <ul style="list-style-type: none"> - 19- nor testosterone. - 17-alpha hydroxy progesterone. - Other as gestoden ... etc |
| General actions | <ol style="list-style-type: none"> 1. Development of 2ry sexual character in females at puberty. 2. Breasts : development of duct system and increased vascularity. 3. Bone: increases bone formation and union of epiphysis. 4. Feed back mechanism: <ul style="list-style-type: none"> - Negative feed back effect on FSH (inhibition of ovulation). - Positive feed back effect on LH (LH surge). 5. Salt and water retention. | <ol style="list-style-type: none"> 1- Hypothalamus (heat regulating centre) thermogenic effect. 2- Breasts: development of alveolar system. 3- Smooth muscles: relaxing effect. 4. Feed back mechanism: negative feed back effect on LH (inhibition of ovulation). 5- salt and water retention. |
| Specific actions | <p>Uterus :</p> <ul style="list-style-type: none"> - Increased vascularity. - Myometrial hypertrophy. - Endometrial proliferation. - Increases the sensitivity of the uterus to oxytocin (increases frequency of uterine contractions). <p>Cervix : (physiology of Menstruation).</p> <p>Tubes: increases tubal motility.</p> <p>Vagina : (see infection)</p> | <p>Uterus:</p> <ul style="list-style-type: none"> - Endometrium : excretory change in estrogen primed endometrium. - Increases the amplitude of uterine contraction but decrease the frequency. - The isthmus uteri: increases its tone. <p>Cervix:</p> <p>Tubes: decreases tubal motility.</p> |
| Indications | <ul style="list-style-type: none"> - Menopausal syndrome - Amenorrhea and oligomenorrhea - Infertility: cervical factor. - Dysfunctional uterine bleeding - Spasmodic dysmenorrhea - Endometriosis (combined contraceptive pills). - Contraception. - Prolapse: trophic ulcers - Infection: sometimes needed in <ul style="list-style-type: none"> - Vulvovaginitis in children. - Senile vaginitis. - Pruritus vulvae. | <ul style="list-style-type: none"> - Menopausal syndrome. - Amenorrhea and oligomenorrhea - Infertility: Luteal phase defect. - Dysfunctional uterine bleeding - spasmodic dysmenorrhea - Endometriosis - Contraception (combined contraceptive pill or alone). - Endometrial carcinoma: palliative treatment - Habitual abortion and threatened abortion. |
| Methods of applications | <p>see HRT</p> | <p>Oral route :</p> <ul style="list-style-type: none"> - Micronized progesterone. - synthetic progestagens <p>Non oral routes:</p> <ul style="list-style-type: none"> - Intramuscular: 17-alpha hydroxy progesterone caproate. - Vaginal pessaries or rectal suppositories. - Progesterone releasing IUCD. |

Operative & Diagnostic Gynecology

Colposcopy

The colposcope is a stereoscopic binocular microscope which magnifies the cervix 6-40 times. In routine practice a magnification of 16 is used. In this way, the epithelial and vascular changes associated with preinvasive or early invasive cancer of the cervix can be detected. The site of biopsy can be effectively chosen. The colposcope can be used also to study lesions of the vagina and vulva.

Indications:

1- In CIN (mainly), VAIN and VIN when cytology is +ve:

To obtain a directed biopsy (the main aim) + evaluate the extent and degree of the lesion, and differentiates inflammatory atypia from neoplasm and may also differentiate invasive from preinvasive lesions.

2- Evaluate patients with persistent abnormal cytology after treatment of preinvasive and invasive lesions.

3- Evaluate patients exposed to diethylstilbestrol in-utero every year (to detect adynosis).

4- Diagnosis of vagino-cervicitis (hyperemia+ punctuated blood vessels),

5- True erosions (areas of denuded epithelium) and metaplasia.

6- Human papilloma virus (HPV): exophytic lesions +koilocytes especially flat and inverted condyloma.

7 - Atrophic epithelium: thin + the vascular pattern.

Technique:

- Outpatient procedure.
- Must be done after Pap. Smear.
- Clean the cervix from mucous, wash the cervix with saline ± green filter (blood vessel contrast).
- The cervix is examined before and after application of 3% acetic acid and/or Schiller iodine [I2 (2gm) + KI (4gm) + distilled water (300ml) i.e., 1:2:300]
- Acetic acid accentuates the vascular, and epithelial alterations characteristic

The columnar epithelium of the cervical canal appears as irregular surface with long papillae and looks like a bunch of grapes.

The normal squamous epithelium covering the cervix appears smooth, pink and does not change in color after the application of acetic acid.

The Transformation Zone (TZ), which is the junction between the columnar and squamous epithelium is identified by:

- 1- Tongues of squamous epithelium,
- 2- Gland openings and
- 3- Nabothian follicles

Colposcopic findings:

A- Normal colposcopic findings:

No acetowhite areas + normal blood vessels + all stained by iodine.

B- Abnormal finding (mainly found in TZ):

- 1- leukoplakia.
- 2- Acetowhite area appears white after application of 3 % acetic acid.

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- 3- Unstained areas by I2 due to lack of glycogen in the malignant cells.
- 4- Abnormal blood vessels.

C- Unsatisfactory:

The squamo-columnar junction (T.Z.) is not entirely visible i.e., higher lesion is not excluded (usually in postmenopausal females).

Unsatisfactory results are managed by:

- Endocervical curettage using Kevorkian curette or
- Hysteroscopy or
- LETZ (loop Excision of T.Z.).

D- Miscellaneous colposcopic findings:

- 1- Inflammatory changes.
- 2- Atrophic changes.
- 3- True erosion.
- 4- Condyloma.

Laparoscopy

Idea:

Visualization of the peritoneal cavity by endoscope introduced through the abdomen.

Indications:

(A) Diagnostic: Laparoscopy very useful in diagnosis of the following:

1- Infertility.

2- Amenorrhea:

- PCO.
- Streak gonads.
- Ovarian biopsy: Sometimes needed to diagnose resistant ovary syndrome.
- Absent uterus or severe hypoplasia.

3- Ectopic pregnancy especially:

- Undisturbed ectopic.
- Pregnancy of unknown location.

4- Endometriosis:

- Implants: fresh or old.
- Cysts: site, size.
- Adhesions: extent, thickness, site especially in Douglas pouch.
- According to these findings, a scoring of endometriosis can be made.

5- Pelvic tuberculosis.

6- Chronic pelvic pain: To determine the etiology e.g.:

- Pelvic endometriosis.
- Pelvic adhesions.
- Varicosities of the broad ligament.
- Chronic ectopic.

7- Uterine perforation: For the site, size and the presence of active bleeding. A decision of laparotomy may be made accordingly.

8- Second look laparoscopy: May replace second look laparotomy for assessment of completion of treatment of ovarian tumors in clinically free patients.

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(B) Therapeutic:

Operative laparoscopy requires additional puncture sites (2nd, 3rd through which the instruments are introduced).

1- Extraction of a missed IUD: From the peritoneal cavity.

2- Tubal sterilization.

3- Salpingolysis and adhesiolysis: Cutting thin adhesions around tube or in pelvis.

4- Treatment of tubal ectopic (only stable patients): Salpingostomy or salpingotomy.

5- Treatment of endometriosis:

- Destruction of endometriotic foci by electrocautery, laser or endocoagulator.
- Aspiration and lavage or removal of endometriotic cysts.
- Adhesiolysis.

6- GTFT and ZIFT (not nowadays)

7- Surgical staging of genital tract malignancies.

Technique:

- Anesthesia.
- Trendelenberg position.
- Sterilization of (abdomen- vulva).
- Catheterization.
- Bimanual examination.
- Post. wall vaginal speculum.
- Grasp the cervix by vulsellum.
- Introduce canula into the cervix.
- Pneumoperitoneum (2-3L of CO₂) is introduced into peritoneal cavity by versus needle at lower edge of umbilicus.
- Insertion of laparoscope:
 - Trocar and cannula is introduced.
 - Trocar is removed.
 - Laparoscope introduced.
 - Connect light source.

Contraindications:

- Severe cardiopulmonary disease, because CO₂ may cause arrhythmia and the patient's position limits movement of the diaphragm.
- Extensive abdominal scar: The bowel may be adherent to abdominal wall.
- Extensive abdominal hernias or diaphragmatic hernia.
- Previous peritonitis.
- Marked obesity.

Advantage of operative laparoscopy:

- Minimal hospital stay and early return to work.
- Minimal patient discomfort.
- Minimal patient adhesion and therefore minimal iatrogenic infertility.
- Better cosmetic results.
- Rare wound complications.
- Allow proper inspection and excludes the need for what is called exploratory laparotomy.

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Complications:

- 1- Complications of the anesthesia (general or local anesthesia).
- 2- Complications of the uterine manipulator e.g. uterine perforation and infection.
- 3- Complications of Verre's needle:
 - Injury of bowel, blood vessels, abdominal wall haematoma, urinary bladder and ureters.
 - Failure to enter the peritoneal cavity, and if insufflation is done in this case emphysema results.
- 4- Complications due to pneumoperitoneum:
 - Air (gas) embolism.
 - Acidosis (from CO₂), leading to cardiovascular respiratory embarrassment.
 - Transient shoulder pain.
 - Aggravation of existing hernia (due to intra- abdominal pressure).
- 5- Complications of trocar:
 - Injury of bowel: in this case do not remove the trocar and open the abdomen while it is in, because if you remove the trocar you cannot determine the injured site (if injury by Verre's needle ~ no problem).
 - Injury of blood vessels (rarely the aorta and pelvic blood vessels), haemorrhage and haematoma.
- 6- Complications of operative procedures:
 - Diathermy may burn the skin, abdominal wall, intestine, ureter, urinary bladder.
 - Haemorrhage (primary or secondary) and faring up of pelvic sepsis.
 - Laser complications: as diathermy.
- 7- Complications of methylene blue test as complications of tubal patency tests.
- 8- Delayed complications:
 - Wound infection and omental hernia at puncture site.
 - Implantation of endometriosis at puncture site.

Role of laparoscopy in oncology:

- Operative for stage I ovarian, endometrial and cervical carcinoma ± lymphadenectomy.
- Second look laparoscopy after treatment of ovarian malignancy,
- Laparoscopic assisted radical vaginal hysterectomy.
- Lymphadenectomy (pelvic+ para-aortic lymphadenectomy).
- Assisted radical vulvectomy (inguinal lymphadenectomy can be done by laparoscope).
- Diagnosis and treatment of adnexal mass.

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Hysteroscopy

Idea:

Telescope introduced through the cervical canal for panoramic visualization of the uterine cavity.

Indications:

A) Diagnostic indications

I. Gynecological Indication:

1- infertility:

Uterine factor: congenital uterine anomalies, Asherman syndrome, SMF polyp.

2. In post-operative assessment of uterus: metroplasty or myomectomy.

3- In habitual abortions.

4- Irregular uterine bleeding: SMF, endometrial hyperplasia.

5- Missed I.U.D.: Intrauterine or extrauterine I.U.D. (A-P and lateral view of HSG).

6- Examination of virgin:

- Through intact hymen to detect foreign body.
- In children to detect sarcoma botryoids.

II. Obstetric Indications:

Sometimes in post-partum hemorrhage or post abortive bleeding.

B) Therapeutic indications

- Hysteroscopic resection of a uterine septum.
- Hysteroscopic lysis of intra-uterine adhesions.
- Hysteroscopic polypectomy.
- Hysteroscopic myomectomy of submucous fibroid.
- Hysteroscopic endometrial ablation in cases of bleeding and the patient is not surgically fit.
- Hysteroscopic removal of missed I.U.D.
- Hysteroscopic tubal sterilization.

Contraindications:

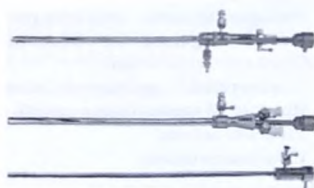
- Suspected pregnancy.
- Genital tract malignancy.
- During menstruation.
- Genital infections.

Technique:

- General anesthesia: in cases of operative hysteroscopy (10 mm in diameter)
- N.B. Not required in cases of diagnostic hysteroscopy (4 mm in diameter).
- Lithotomy position.
- Bladder evacuation.
- Cervical dilatation: in therapeutic hysteroscopy.
- The uterine cavity is distended with distension media e.g. Glycine, saline, CO₂ ... etc.
- The telescope is connected to a light source.

Complications:

- Anesthetic complications (if used).
- Perforation.



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- Haemorrhage.
- Infections.
- Thermal trauma to adjacent structures.
- Complications due to distension media: pulmonary embolism 1 allergy, dilutional hyponatremia ... etc.

Hysterectomy

Types of hysterectomy:

- Abdominal hysterectomy
- Vaginal hysterectomy
- Laparoscopic hysterectomy
- Laparoscopic assisted vaginal hysterectomy

Types of abdominal hysterectomy:

- Subtotal hysterectomy: The body of uterus is removed but the cervix is left.
- Total hysterectomy: The body of the uterus and cervix are removed.
- Pan hysterectomy: Total hysterectomy and bilateral salpingo-oophorectomy.
- Extended hysterectomy: Total hysterectomy + removal of the medial portions of cardinal ligaments + removal of upper 2cm of the vagina.
- Radical hysterectomy e.g. Wertheim's operation (see cancer cervix).
- Extended radical hysterectomy: Pelvic exenteration (see cancer cervix).
- Caesarean hysterectomy: Removal of the uterus after C.S.

Indications:

I. Gynecological Indication

- Tumors:
 - Benign tumors as fibroids and benign ovarian tumors in old age.
 - Malignant tumors as cancer cervix, endometrium, ovary.
- Dysfunctional uterine bleeding: in some cases (see DUB).
- Endometriosis and adenomyosis: in some case (see endometriosis).
- Prolapse: in some cases (see prolapse).
- Infections: genital TB infection, chronic PID in old aged women.

II. Obstetric Indications

- Uncontrollable postpartum hemorrhage
- Rupture of uterus (some cases).
- Placenta accreta
- Couvelaire uterus.

Advantages of Subtotal Hysterectomy

- Easy and takes a shorter time than total hysterectomy.
- Less liability to injure the bladder, ureter and rectum.
- The cervix is not removed and this guards against vault prolapse.
- It is not followed by dyspareunia.

Disadvantages of Subtotal Hysterectomy

- Risk of cervical stump carcinoma (0.1-1%).

Disadvantages of Total hysterectomy:

- Difficult and takes longer time than subtotal hysterectomy.
- More liability to injure the bladder, ureter and rectum.

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- More risk of pelvic infection (the vagina is opened).
- More risk for vault prolapse.
- It is followed by dyspareunia (absence of lubricating cervical secretion).

Advantages of Total Hysterectomy

- No risk of cervical stump carcinoma.
- Better drainage of the pelvis after the operation. (the vagina is opened)

Steps for abdominal hysterectomy:

- Preparation, catheterization, anesthesia, sterilization and toweling.
- Division and ligation of the round ligaments.
- Division and ligation of the tubes and ovarian ligaments flushing with the uterus if the ovaries are to be preserved or clamping and cutting the infundibulo-pelvic ligament if the ovaries will be removed.
- Dissect the bladder downwards, by blunt and sharp dissection.
- Clamping and ligation of the uterine vessels.
- Clamping and ligation of Mackenrodt's ligament and uterosacral ligaments.
- Opening of the upper vagina usually from the anterior (but can be from the lateral or posterior surface), divide the vagina from its attachment to the cervix all around to remove the uterus.
- Vaginal vault is closed by interrupted suture (some do under-running of edges and leave the vagina open). Stumps of cardinal and uterosacral ligaments are included in vaginal vault to support it to guard against vault prolapse.
- Closure of the abdomen as usual.

Complications of abdominal hysterectomy:

Intraoperative:

- **Anesthetic complications:** according to the type of anesthesia.
- **Shock:** Anaesthetic or neurogenic (excess pain) or hypovolaemic.
- **Haemorrhage:** (1ry hemorrhage) due to:
 - Slippage of uterine artery managed by bilateral internal iliac artery ligation.
 - Injury of internal iliac blood vessels, needs vascular surgeon.
- **Injuries:**
 - i- Urinary bladder injury usually direct trauma or misplaced suture leading to vesico-vaginal fistula.
 - ii- Ureteric injury.
 - iii- Intestinal injury:
 - If small intestine, do resection anastomosis.
 - If large intestine, do temporary colostomy to be closed latter on after preparing the patient.

Postoperative complications:

- **A- Early:**
 - 1- **DVT and pulmonary embolism.**
 - 2- **Reactionary hemorrhage:** (within 24 hours) due to slipped ligature.
Or **Secondary hemorrhage:** (on the 7th or 10th day post-operative)
 - Usually due to infection and very difficult to treat.
 - Usually treated by strong antibiotics and bilateral internal iliac artery ligation ± pack.

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3- Infections:

- Respiratory tract infections (inhalation during anesthesia).
- Peritonitis due to infection during operation or spread from vagina or wound leading to paralytic ileus and septic shock.
- Urinary tract infection (catheter).
- Wound infection.

4- GIT: Acute gastric dilatation, stress ulcer and paralytic ileus.

5- Wound: Burst abdomen due to disruption of all layers especially in longitudinal incision (weak healing) and hematoma.

• B- Late:

- Post-hysterectomy syndrome (Psychologic): As the females consider hysterectomy loss of femininity ↓ libido and lack of interest. It is treated by proper counseling.
- Vault prolapse.
- Acute menopausal symptoms if both ovaries are removed.
- Pelvic and abdominal adhesions.

Vaginal hysterectomy

Indications of vaginal hysterectomy:

- Uterine prolapse: (see prolapse).
- Dysfunctional uterine bleeding.
- Fibroid uterus and adenomyosis provided that size of the uterus isn't more than 12 weeks pregnancy.
- Shauta's radical vaginal hysterectomy, in cervical carcinoma stages Ib and IIa (not done).
- Some cases of chronic inversion of the uterus.

Advantages of vaginal hysterectomy:

- No abdominal scar and incisional hernia.
- No post-operative respiratory discomfort.
- Rare incidence of intestinal distension, peritonitis, adhesions and intestinal obstruction.
- Any associated prolapse of the vagina can be corrected at the same sitting.

Disadvantage of vaginal hysterectomy:

- unsafe if there is pelvic adhesions.
- The ovaries are difficult to be removed.
- Difficult if size of the uterus is > 12 weeks (can be bisected before removal in large uterus).
- Risk of vault prolapse is more than after abdominal hysterectomy.

Steps:

- Preparation, anesthesia, vaginal sterilization, toweling and lithotomy position.
- The vagina is opened at its attachment with the cervix with cricular or inverted-T incision.
- Dissect bladder upwards after cutting pubo-cervical ligament.
- Open the peritoneum of Douglas pouch and that of the vesico-vaginal pouch.

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- Clamp and cut from below upwards on both sides: Mackenrodt's ligament utero-sacral ligament, uterine vessels, broad ligament, then the tubes and ovarian ligaments or the infundibulo-pelvic ligaments (if ovaries are to be removed), and remove the uterus.
- Close the vagina by interrupted or continuous locked sutures with attachment of the Mackenrodt's ligament and uterosacral ligament to support the vaginal vault (cut redundant vagina anteriorly before closure if the vaginal incision is extended up to do vaginal repair).
- Posterior colpo-perineorrhaphy is done if there is posterior vaginal wall prolapse.
- Vaginal pack and catheter to be removed after 24 hours(to prevent reactionary hge).

Complications of vaginal hysterectomy:

As simple hysterectomy, but all complications are less except:

- Pelvic cellulitis.
- Reactionary hemorrhage (bad pedicle securing) leading to pelvic haematoma.
- Secondary hemorrhage which is treated by pack and antibiotics. If failed internal iliac artery ligation is to be done.
- Vault prolapse or enterocele.
- Stress incontinence (due to vigorous dissection).
- Injury of the rectum (very rare), over-stenosis of the vagina or vault granulation leading to dyspareunia.

Laparoscopic hysterectomy

Advantage over laparotomy:

- Small skin incision, less pain and more cosmetic.
- Less tissue trauma.
- Less hospital stay, rapid convalescence and less cost.
- Less blood loss.

Indications:

- Benign pathology e.g. endometriosis, fibroid or adnexal mass.
- Malignancy stage I ovarian carcinoma, endometrial and cervical malignancy with addition of lymphadenectomy.

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Dilatation and Curettage

Types of dilators:

1- Hegar dilator has a uniform thickness throughout its whole length.

2- Fenton dilator tapers gradually towards the tip.

The number indicates the diameter in mm e.g. Hegar number 4 = 4 mm in diameter.

Indications:

1- Dilatation alone:

- Spasmodic dysmenorrhea
- Cervical stenosis.
- Drainage of pyometra or hematometra.

2- Dilatation preliminary to another procedure:

Cervical procedures:

- Amputation (including Fothergill operation).
- Tracheorrhaphy
- Cautery in nullipara.

Uterine procedures:

- Curettage and evacuation
- Polypectomy.
- Introduction of radium.

Technique:

- General anesthesia.
- Lithotomy position.
- Sterilization of the vulva, vagina and skin.
- Application of sterile towels.
- Catheterization to evacuate the bladder.
- Bimanual examination for the size, direction and masses of the uterus and adnexa.
- Posterior vaginal wall speculum is applied and the anterior lip of the cervix is pulled by a volsellum.
- Sounding of uterus to detect size and direction of the uterus.
- Dilatation of the cervix:
- Usually starting by dilator number 3 or 4.
- The dilator is held like a pencil and pushed gently through the cervical canal. The 1st resistance is felt at the internal os and then it is pushed through the cervix. The dilator should be left for 30 seconds to allow the circular fibers to relax.
- Then removed and the next larger size is introduced until the required dilatation.
- Number 8-10 for endometrial curettage.
- Number 12 before amputation of the cervix.
- Number 14 for treatment of spasmodic dysmenorrhea.

Types of curettes:

- 1- Loop curette, which is either sharp or blunt: Blunt curette is used if uterus is liable to perforation e.g. malignancy or recent pregnancy.
- 2- Biopsy curette e.g. Novak or Sharman curettes:
 - Anesthesia and cervical dilatation are not needed as the curette has a small diameter.
 - Used to obtain small endometrial strip e.g. detection of ovulation. Thus, it is not suitable for to detect malignancy.

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- 3- Fundal curette: has a tapering end to curette fundus and angles.
- 4- Flushing curette (Rheinstader curette): Used to curette and at the same time to wash the decidua after evacuation.

Indications:

- 1- Diagnostic (endometrial biopsy):
 - Detection of ovulation by dated premenstrual endometrial biopsy.
 - Detection of luteal phase defect by a dated premenstrual endometrial biopsy.
 - Detection of TB endometritis
 - Detection of cancer of the endometrium or endocervix by fractional curettage.
 - Differentiation of DUB and organic causes of uterine bleeding.
- 2- Therapeutic:
 - Postpartum and post-abortive hemorrhage to remove retained products.
 - Endometrial and cervical polyps. c- Dysfunctional Uterine Bleeding (DUB).

Technique:

Dilatation: is done first under anesthesia up to number 8-10 Hegar.

Curettage: The endometrium is scraped till a gritty sensation is felt Starting with anterior then the posterior walls. The fundus and lateral walls are then scraped. In fractional curettage, the cervix is curetted before dilatation of the cervix.

Complications of dilatation and curettage:

- 1- Complications of anesthesia.
- 2- Shock due to:
 - Dilatation without or with improper anesthesia (vasovagal attack).
 - Excessive bleeding.
- 3- Injury and hemorrhage due to:
 - a- Cervical lacerations:
 - Liable with very rapid and excessive cervical dilatation more than number 12.
 - Complications: Hemorrhage due to injury of cervical branch of the uterine artery, Infection i.e. cervicitis and incompetent isthmus.
 - Treatment: Suturing of the tear.
 - b- Perforation of the uterus:
 - ❖ Predisposing factors:
 - Perforation occurs by the sound, dilator or curette specially in the following:
 - Retroverted or acutely ante-flexed uterus.
 - Soft uterus due to pregnancy.
 - Friable uterus due to malignancy or severe infection.
 - ❖ Dangers:
 - Hemorrhage.
 - Infection.
 - Injury of the intestines or omentum.
 - Rupture of the scar in a subsequent pregnancy.
 - ❖ Diagnosis:
 - Sudden release of resistance.
 - Vaginal bleeding.
 - Introduction of the sound or dilator beyond the expected length of the uterus.
 - Prolapse of intestines or omentum if the perforation is large.
 - ❖ Prevention is the most important:

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- Evaluation of the size, direction and consistency of the uterus before dilatation.
- Straightening of the uterus by traction on the cervix using a volsellum.
- Holding the dilator in the proper way like a pencil and avoiding excessive force.

❖ Treatment:

- i. Observation: Operation is stopped. Vital signs and signs of internal hemorrhage are observed. Usually the perforation is small and interference is not needed.
- ii. Antibiotics are given.
- iii. Laparotomy: Indicated in the following conditions:
 - Abdominal contents prolapse through the perforation.
 - Excessive vaginal bleeding.
 - Evidence of internal hemorrhage.
 - Septic abortion or pyometra.
 - In cases of malignancy.
- iv. The uterus is repaired or removed if the tear is irreparable.
- v. The intestine, omentum should be inspected for any injury, that should be repaired.
- vi. iv. If bleeding is slight and the patient is not shocked:
 - Ergometrine and antibiotics are given.
 - Evacuation can be completed guided by laparoscopy.

4- Infection.

5- Remote complications:

- Incompetent isthmus is a complication of dilatation only.
- Asherman syndrome is a complication of curettage and not dilatation.
- Rupture uterus in subsequent pregnancy if perforation occurs.

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Myomectomy

Indications:

- It is the operation of choice in all women below the age of 40 who want to become pregnant.
- A small fibroid polyp not larger than 8 weeks pregnancy is removed by vaginal myomectomy.
- A submucous fibroid less than 5cm in diameter is removed using the hysteroscope.

Contraindications:

- If the patient is above the age of 40.
- Blocked tubes as bilateral hydrosalpinx or pyosalpinx because it is useless to leave behind the uterus as the patient will be sterile, unless IVF and ET is planned for.
- Multiple fibroids if it is found that the operation will leave behind a useless organ.
- Cervical fibroid is usually treated by hysterectomy.
- If malignancy is suspected.
- The presence of other lesions in the uterus as adenomyosis.

N.B: A written consent for hysterectomy should be obtained from the patient and husband before myomectomy as hysterectomy may be needed during the operation (3%).

Types:

- Abdominal myomectomy.
- Vaginal myomectomy.
- Laparoscopic myomectomy.
- Hysteroscopic myomectomy.

Preoperative evaluation:

- Complete history and physical examination.
- Complete blood count. Hemoglobin should not be less than 11 gm%.
- Ultrasonography if not already done.
- Endometrial biopsy or uterine curettage is done if there is irregular uterine bleeding to exclude endometrial carcinoma.
- If infertility is a complaint, all investigations of infertility including hysterosalpingography are carried out to exclude another cause of infertility and to confirm tubal patency.
- Hysteroscopy may be used to diagnose a submucous fibroid or a small fibroid polyp.
- Intravenous pyelogram is done in case of cervical and broad ligament tumour to show the course of the ureter, to diagnose hydroureter and hydronephrosis and to assess kidney function.
- Other investigations to prepare the patient for operation.
- A written consent for hysterectomy should be obtained from the patient and husband as hysterectomy may be needed during operation.

Methods to reduce blood loss during myomectomy:

a) Preoperative measures:

- Correction of anemia. Hemoglobin should not be less than 11 gm%.
- If patient is taking Aspirin it should be stopped at least 2 weeks before operation.

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- A gonadotrophin releasing hormone analogue may be given for 3 months before operation. It corrects anaemia by causing amenorrhoea. It reduces the size and vascularity of the myomas and so the operation becomes easier and with less blood loss.
- Operation is done in the postmenstrual period when there is no pelvic congestion.

b) Measures during operation:

- Anesthetics that cause uterine relaxation are better avoided.
- An ampoule of ergometrine (0.25 mg) may be given intravenously at the start of operation.
- Injection of vasopressin (pitressin) in the uterine wall at the site of incisions (one ampoule 20 units diluted with 20 ml normal saline or Ringer lactate solution).
- The use of Bonney myomectomy clamp or a rubber catheter to surround the lower part of the uterus to compress the uterine arteries to minimize blood loss.
- The use of ring forceps to occlude the ovarian arteries in the infundibulopelvic ligaments.
- The use of a vertical incision in the midline which is the least vascular area.
- Minimize the number of incisions in the uterus.
- Removal of the tumour through the proper plane within its capsule.

Technique of abdominal myomectomy:

- The abdomen is opened by a midline subumbilical incision reaching just above the upper border of symphysis pubis or by a transverse suprapubic (pfannenstiel) incision.
- After exploration, the uterus is delivered out of the wound.
- A Bonney myomectomy clamp or a rubber catheter is applied to surround the lower part of the uterus to compress the uterine arteries to minimize blood loss during operation. A ring forceps may also be applied to each infundibulopelvic ligament. Ergometrine can be given IV at the start of operation or vasopressin (pitressin) may be injected into the uterine wall.
- The uterine wall is incised and the myoma is removed from its capsule using traction with the vulsellum or myoma screw.
- In case of multiple tumours, the incision is made to remove the maximum number through the same incision, and small tumours can be removed by tunneling.
- The best incision is in the midline of the anterior wall of the uterus to minimize bleeding and to avoid postoperative adhesions to the omentum and intestine. For the last reason, a posterior wall fibroid is removed by a transcavitary incision, or by Bonney hood technique, where a transverse incision is made in the fundus just away from the fallopian tubes, the flap is dissected downward to remove the tumour and then the redundant flap (hood) is brought forward over the fundus and sutured to the anterior wall. In some cases, the posterior wall fibroid is removed by a direct incision over the tumour.
- The uterine cavity is not opened to avoid formation of intrauterine adhesions; however, if there is a submucous fibroid the cavity is opened to remove the tumour.
- The cavities are obliterated by chromic catgut or delayed-absorbable sutures as Vicryl.
- Finally, the clamp or rubber catheter is removed and the uterus inspected to be sure of haemostasis.
- The round ligaments are plicated or sutured together in front of the uterus to prevent retroversion and postoperative adhesions between the intestine and anterior wall of uterus. Placation of uterosacral ligaments also prevents retroversion.

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Complications of myomectomy:

I) During operation:

- Primary hemorrhage.
- Injury to the bladder, ureter, fallopian tubes, and intestine.
- Anesthetic complications as Mendelson syndrome due to aspiratin of vomitus.

II) Postoperative complications:

- **Cardiovascular:** Reactionary and secondary hemorrhage, venous thrombosis.
- **Pulmonary:** As bronchitis, pneumonia, and lung atelectasis.
- **Gastrointestinal tract:** Postoperative distension, vomiting, acute gastric dilatation, paralytic ileus and peritonitis. Later adhesions and intestinal obstruction.
- **Complications in the abdominal wound:** Infection, burst abdomen, and incisional hernia. Incisional hernia is very rare after Pfannenstiel incision (1 in 1250 cases).
- **Intrauterine adhesions (Asherman syndrome)** if the uterine cavity is opened.
- **Persistence of menorrhagia (1-5%)** due to missed fibroids, endometrial hyperplasia, cystic changes in the ovaries.
- **Recurrence of fibroids** in 10-25% of cases within 10 years due to missing small fibroids at operation, or the growth of new tumors.
- **Rupture of the uterine scar** in subsequent pregnancy or labor.

Vaginal myomectomy

- It is indicated for a small fibroid polyp not larger than 8 weeks pregnancy.
- The tumour is grasped by a vulsellum and twisted until the pedicle tears.
- The bleeding is usually slight or absent. If the pedicle is thick it is cut with scissors.
- A large polyp can be removed vaginally by cutting it piece-meal (morcellation).

Laparoscopic myomectomy

The laparoscope can be used to remove subserus and interstitial fibroids, up to 10 cm in diameter, but not submucous tumors.

Hysteroscopic myomectomy

- A fibroid polyp inside the uterine cavity can be removed by the operative hysteroscope.
- A submucous myoma less than 5 cm in diameter is resected (by the diathermy loop of the hysteroscope (resectoscope)).
- Hysteroscopic myomectomy avoids abdominal and uterine incisions and shortens hospital stay.

N.B: Myomectomy has a higher mortality rate than hysterectomy because of the risk of hemorrhage which may occur from the tumor bed.

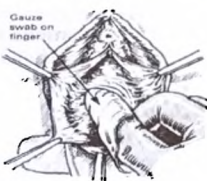
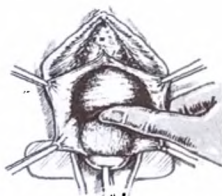
IX. Operative & Diagnostic Gynecology

Prolapse operations

Anterior Colporrhaphy:

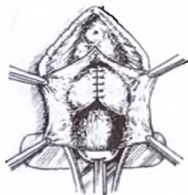
1. The anterior vaginal wall is separated from the bladder.
2. The bladder is pushed upwards to its original position as a pelvic organ behind the symphysis pubis.
3. The fascia between the bladder and vagina is sutured in the midline to form a shelf below the bladder.
4. Redundant vaginal wall is removed and the vagina is closed in the midline.
5. Chromic catgut or delayed absorbable sutures as Vicryl are used for repair.
6. Foley catheter and a tight vaginal pack are usually inserted and left for 24 hours. The pack helps haemostasis and prevents reactionary haemorrhage.

NB: The fascia between the bladder and vagina is difficult to identify and it has various names: pubovesical fascia, pubocervical ligaments or fascia of Denon Villiers.



Posterior coloperineorrhaphy:

- The posterior vaginal wall is separated from the rectum.
- The two levator ani muscles are approximated in the midline in front of the rectum.
- Redundant vaginal wall is removed and the vagina is closed.
- The superficial perineal muscles are sutured together in the midline and the skin is closed.
- Finally, a Foley catheter and a tight vaginal pack are usually inserted and left for 24 hours.



Fothergill (Manchester) Operation

It is indicated for combined vaginal and uterine prolapse when there is supravaginal elongation of the cervix or when it is lacerated or infected.

Steps:

- A uterine sound is passed to measure the length of cervix to estimate the length to be amputated.
- Dilatation and curettage. Dilatation is necessary to allow covering the raw area left after amputating the cervix. Curettage to remove the congested endometrium, to reduce the amount of subsequent menstruation, and to exclude any endometrial pathology.
- Anterior colporrhaphy to correct the cystocele.
- Amputation of the cervix to restore its normal length which is one inch.
- The Mackenrodt ligaments are sutured together in front of the cervix. This shortens the ligaments and elevates the uterus upwards, also the cervix is pulled backwards to correct retroversion.
- The raw area of the cervical stump is covered by mucosa.
- Posterior coloperineorrhaphy is then performed.

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NB: If the cervix is not elongated, infected or lacerated the case is treated by modified fothergill operation that is without amputation of the cervix (anterior repair + suturing Mackenrodt ligaments in front of cervix + posterior repair).

Complications:

- The operation takes a long time.
- There is excessive blood loss throughout the operation.
- Injury of urinary bladder, ureter or rectum.
- High amputation of the cervix may lead to abortion or recurrent preterm labour due to cervical incompetence.
- Subsequent fibrosis in the cervix may lead to infertility, dysmenorrhoea, hematometra or failure of the cervix to dilate during labour (cervical dystocia).
- Dyspareunia due to narrowing of the vagina or tender scar.

Sling Operations

- Used for congenital uterine and vault prolapse.
- Non-absorbable material as prolene type is used to suspend the cervix or vault of vagina to the anterior spinal ligament of the sacrum.
- Vault prolapse can also be treated by fixing the vaginal vault to the sacrospinous ligament to one side (transvaginal sacrospinous colpopexy).

Operations for Hernia Of Douglas Pouch

Vaginal repair:

- The posterior vaginal wall is dissected upwards till the posterior fornix.
- The hernia sac is dissected and opened.
- The contents are displaced.
- The neck of the sac is transfixed and ligated and the sac is excised.
- The uterosacral ligaments are sutured together.
- Posterior repair is then performed.

Abdominal repair:

- The Douglas pouch is obliterated by a series of purse string sutures from below upwards using delayed-absorbable sutures as Vicryl.
- The needle bites include the uterosacral ligaments, the posterior wall of cervix and the serous coat of the rectum (Moschowitz operation).
- In Halban operation 5 or 6 stitches are passed in the peritoneum of Douglas pouch from before backwards to obliterate the pouch. This avoids the uterosacral ligaments to avoid injury of ureters.

NB: It is preferable not to treat prolapse until the patient completes her family as vaginal delivery may lead to recurrence of the prolapse.

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Stress incontinence operations

It is the primary treatment of stress incontinence. The operation is done vaginally, abdominally, or Abdomino-vaginal.

A. Vaginal Operations:

Kelly operation:

- It consists of repair of cystocele and/or urethrocele.
- The paraurethral tissue on both sides is then brought to the midline using interrupted sutures. In this way, we plicate the whole urethra and bladder neck. This gives support to the urethra and restores the normal posterior urethrovesical angle.

B. Abdominal Operations:

1. Marshall-Marchetti-Krantz:

- The stitches are placed in the fascia on each side of the bladder neck and upper half of the urethra and are attached to the periosteum on the back of the symphysis pubis.
- This restores the normal intra-abdominal position of the urethra.
- Main complication is osteitis pubis (0.5-5%).
- Non-absorbable (as Mersilene) or delayed absorbable sutures (as Vicryl or Dexon) are used.

2. Burch Operation:

- Burch colposuspension is the operation of choice.
- It corrects both stress incontinence and cystocele.
- The stitches are placed in the fascia on each side of the bladder neck and the base of the bladder and are attached to the iliopectineal ligaments (Cooper Ligaments).
- Non-absorbable or delayed absorbable sutures are used.
- Operation can be done through the laparoscope.
- The success rate of the above abdominal operations is 80-90%.

3. Combined abdominovaginal operations:

Sling operations:

Autogenous fascia (rectus sheath, fascia lata, round ligaments) or synthetic material (nylon, polyethylene) is placed below the bladder neck to form a sling.

1. Aldridge sling operation:

- Two strips from the anterior rectus sheath are brought down behind the symphysis pubis and stitched below the bladder neck.

2. Stamey operation:

- An incision is made in the vaginal wall to expose the bladder neck.
- A nylon suture is placed in the fascia on each side of the bladder neck.
- The two sutures are passed upward behind the symphysis pubis using a special needle and are attached to the anterior rectus sheath.
- The cystoscope is used to be sure that the needle does not pass through the bladder.

Recent lines in management of stress incontinence:

1. Tension-free-vaginal tape (TVT) operation:

- The tape is made of prolene and has a curved needle at each end.
- Operation is done using local infiltration anaesthesia.
- Technique:
 - Two small transverse incisions 5 cm apart are made in the suprapubic area. A vertical incision is made in the anterior vaginal wall.

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- The needles of the tape are passed upward behind the pubic bone and brought out through the suprapubic incisions.
 - The tape is made to surround the mid-urethra.
 - The cystoscope is used by the assistant to make sure that the bladder is not pierced by the needle.
 - The tape is adjusted by pulling on its ends, and continence is confirmed by asking the patient to cough.
 - The ends of the tape are cut off and left free and not fixed to the tissues.
 - Finally the vaginal and suprapubic incisions are closed.
 - Operation takes 20-30 minutes.
 - The cure rate is about 85%.
2. **Transobturator tape (TOT) operation:**
- A synthetic tape (prolene) is passed through the obturator foramen to support the mid-urethra.
 - It avoids bladder perforation which may occur with TVT operation.
 - In TOT the tape is passed through obturator foramen from inside out (O).
3. **Artificial Urinary Sphincter:**
- Indicated when surgery fails to correct stress incontinence.
 - The device consists of a cuff which is placed around the bladder neck.
 - A balloon reservoir, containing fluid is placed in the peritoneal cavity or under the anterior rectus sheath, and a small pump is situated in one labium major.
 - Under normal conditions the cuff is full with fluid thus closing the bladder neck.
 - When voiding is desired, the pump is pressed to force the fluid in the cuff to go back into the balloon reservoir so that voiding can occur. The cuff then gradually refills over the next few minutes.

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Operations for vesicovaginal fistulae

i. Vaginal operations:

1) The flap splitting or dedoublement operation:

The vagina is separated from the bladder and each organ is closed separately.

Technique of dedoublement operation:

- General or spinal anesthesia.
- Posture. The patient is put in the lithotomy position.
- If the vagina is narrow a midline or mediolateral episiotomy (Schushardt incision) is done and closed at the end of operation.
- A circular incision is made in the vaginal wall around the fistula and 0.5cm from its margin. From this incision, two longitudinal cuts are passed upwards and downwards in the vaginal wall.
- The vaginal wall is then separated from the bladder over a wide area, at least 1.5cm all around the fistula.
- The opening in the bladder is closed in 2 layers. Some surgeons excise the fibrous tissue to freshen the edges of the fistula to leave a raw edge for better healing.
- Sterile methylene solution is injected into the bladder to be sure that it is water tight. If any leakage occurs, further sutures are taken.
- The vagina is then closed.
- A Foley catheter is fixed to avoid distension of the bladder.
- A vaginal pack may be inserted at the end of operation to help haemostasis and to avoid reactionary haemorrhage.

2) The saucerization or Sims operation:

- An elliptical incision is made in the vaginal wall.
- The edge of the fistula is excised obliquely removing a wider part of the vaginal than of the muscle wall of the bladder (no mucosa is removed).
- The edges of both organs simultaneously sutured using a single layer of non – absorbable material as nylon or silver wire.
- It is done for high inaccessible fistula surrounded by dense scar tissue as vault fistula after hysterectomy. In this case it is difficult to separate the vagina from the bladder.

3) Latzko operation:

- It has the same indication as saucerization operation.
- A circular incision is made in the vaginal wall around the fistulous opening.
- The tract of the fistula is excised. This allows mobilization of the bladder which is closed.
- This is followed by closure of the vagina.
- In this way the vaginal vault is obliterated (partial colpocleisis).

4) Post-irradiation fistula:

- The blood supply of the area is poor, so we transplant some tissue with intact blood supply between the bladder and vagina.
- We can use the gracilis muscle, the bulbocavernosus muscle (Martius graft) or a flap the rectus abdominis.

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ii. Abdominal operation:

❖ Indicated when:

- Vaginal operations fail
- The fistula is surrounded by excessive fibrosis so separation of bladder becomes difficult,
- High fistula which cannot be reached easily from below.

❖ The abdominal approach may be:

- Extraperitoneal transvesical or
- Intraperitoneal transvesical or
- Intraperitoneal extravesical.

The transperitoneal approach is used when the extraperitoneal approach is difficult or an omental graft is indicated. Pfannenstiel or midline incision. However, if an omental graft will be needed we have to use a midline incision that can be extended enough to allow mobilization of the omental pedicle.

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Radiotherapy in gynecology

Indications:

- Treatment of malignant tumors of the genital tract.
- Induction of artificial menopause.

Mode of application:

- Brachytherapy (internal irradiation).
- Teletherapy (external irradiation).
- Intraperitoneal instillation of radioactive substance as radioactive gold.
- Super-voltage therapy: cobalt-60 or linear accelerator.

Mechanism of action:

- Direct effect: cytolethal.
- Indirect effect: end-arteritis obliterans → ischemia and necrosis of tumor cells.

Methods of application in cancer cervix:

I. Paris technique:

Small dose for long time → 33.3 mg in the uterus and 33.3 mg in the vagina.

II. Stockholm technique:

- High dose for short time → 50mg in the uterus and 60mg in the vagina.
- Then reapplied after 3w.

III. Manchester technique:

- Calculated dose → 7000-8000 rad to point A and 3000 rad to point B.
- Point A is 2cm lateral to the center of the cervix and 2cm above the vaginal vault (correspond to paracervical L.N.).
- Point B is 3cm lateral to point A (correspond to obturator L.N.).

Recent after-loading technique: (computerized dosimetry technique):

The dose is calculated by computer system.

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Gynecologic cytology

The study of cellular character and morphology of desquamated epithelial cells.

Indications:

Gynecologic:

- Screening and follow up of malignancy.
- Evaluation of the hormonal status→ Detection of ovulation.
- Sample is obtained from lateral vaginal wall.
- Maturation index: Percentage of parabasal, intermediate and superficial cells.
- Infections: Vaginitis or HPV.
- Chromatin pattern to detect Barr body: by buccal smear.
- Detection of radio-sensitivity before and after radiotherapy for cervical cancer.

Obstetric:

- Fetal cells indicate premature rupture of membranes.
- Trophoblastic cells indicate abortion.
- Parabasal cells indicate fetal death.
- Intermediate cells < 95% indicates placental insufficiency.
- In normal pregnancy, 95% of the cells are of intermediate (due to progesterone).

Site of cytology:

- Cervicovaginal.
- Endometrium.
- Buccal.
- Ascitic or amniotic fluid.

X. Family Planning

FAMILY PLANNING

Definition:

Prevention of conception by any method except abstinence.

Aims of contraception:

- 1) To prevent overpopulation especially in the developing countries.
- 2) To offer proper pregnancy spacing for the sake of the mother & the baby.
- 3) Prevention of pregnancy in cases where pregnancy is contra-indicated.
- 4) Better nutrition, education and care for children.

Methods of contraception:

- 1- Natural family planning:
 - o Fertility awareness methods.
 - o Coitus interruptus.
 - o Lactational amenorrhea method.
- 2- Hormonal contraception.
- 3- Intrauterine contraceptive devices (IUCD).
- 4- Barrier methods:
 - o Male condom (male sheath).
 - o Female condom.
 - o Vaginal diaphragm (Dutch cap).
 - o Cervical cap.
 - o Contraceptive sponge
- 5- Chemical contraceptives (spermicides).
- 6- Sterilization (permanent contraception):
 - o Male sterilization
 - o Female sterilization.
- 7- Recent methods (under trial):
 - o Male pills (Gossypol).
 - o Progesterone antagonists (Ru 486) Mifepristone.
 - o Immunological methods (Contraceptive vaccine).

Assessment of effectiveness:

1- Pearl index:

Number of pregnancy per hundred women/year in those women at risk of pregnancy/HWY.

$$PI = \frac{\text{Number of pregnancies} \times 1200 \text{ (number of months used by 100 women in 12 months)}}{\text{Total months of use by all women}}$$

So, if 500 women used a contraceptive method for 20 months during which 5 pregnancies occurred, the pregnancy rate is 0.6 per Hundred Women per Year (HWY) calculated as follows:

$$PI = \frac{5 \times 1200}{500 \times 20} = 0.6 \text{ per HWY}$$

2- Method failure:

Failure attributed to the method (the use is under ideal circumstances).

3- Patient failure:

Failure is attributed to less than ideal use of the method.

4- User failure:

Actual failure attributed to the method & patient.

X. Family Planning

NATURAL FAMILY PLANNING METHOD (N.F.P)

1- Fertility awareness method:

Defined by WHO as 'the voluntary avoidance of intercourse by a couple during the fertile phase of the menstrual cycle in order to avoid a pregnancy'.

Failure rate: 2- 20/HWY.

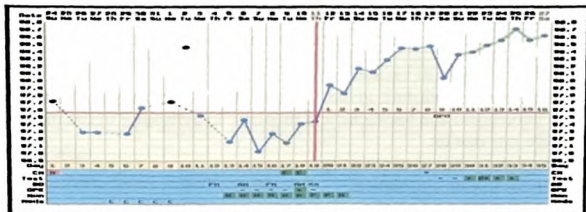
Mechanism: Avoiding coitus during fertile times in the menstrual cycle is based on three facts:

1. Ovulation occurs 12-16 days before the onset of next menses (Rule of Ogeno).
2. Spermatozoa are capable of fertilization only for 2-3 days.
3. Ovum is capable of fertilization for only 24 hours post ovulation.

Methods:

1- The calendar or rhythm method:

- Record of 6 -12 cycles is done & the shortest and longest cycles are defined.
- The 1st day is calculated by subtracting 18 days from length of the shortest cycle & the last day is calculated by subtracting 11 days from the longest cycle.



2- The basal body temperature method:

- It relies on the thermogenic effect of progesterone in the 2nd half of the cycle.
- Female is considered fertile from the beginning of the cycle till 3 days after the rise of temperature.

3- The cervical mucus method (Billing method, Ovulation method):

Whereby a woman identifies when she is fertile by noting changes in the appearance and texture of the cervical mucus.

4 phases are recognized:

- 1- The **dry days** following menstruation, thick cervical mucous plug.
- 2- Early pre-ovulatory phase, the **dry sensation disappears**.
- 3- The **wet days**, prior to ovulation, when mucous become more copious and clear.
- 4- The **dry vagina**, where the mucous becomes sticky, cloudy and scanty.

Intercourse can take place in the dry days following menstruation and after the 4th day after the peak of mucus.

4- The symptom-thermal method:

- **Combination of symptoms** (cervical. mucus) & Thermal method (BBT-Chart).
- **Recently**, modified to **double check method**.

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Advantages of fertility awareness methods:

- No disturbance to normal physiology.
- Readily available.
- Safe.
- Morally & socially accepted.

Disadvantages of fertility awareness methods:

- Needs highly motivated couples.
- Signs of fertility may not be reliable.
- Needs cooperation of both couples.
- No STI/HIV protection.
- High use failure rate 2 – 20/ HWY. (the safe period is unsafe!).
- Cannot be applied except in regular cycle.

New Technology in N.F.P.:

- Hormone level in saliva.
- Double check method.
- Urinary dip stick for LH (Persona).

2- Coitus interruptus:

Withdrawal of the penis just before ejaculation.

Disadvantages:

- 1- May interfere with sexual satisfaction.
- 2- Pelvic congestion syndrome in the female with menorrhagia, increased normal vaginal discharge (leucorrhoea) and backache and prostatic hypertrophy in the male.
- 3- High failure rate due to:
 - The pre-ejaculatory mucus contains spermatozoa.
 - Lack of self-control on ejaculation.
 - Few drops of semen escape before ejaculation.
 - Not suitable for male with premature ejaculation or lack of sex control.

3- Lactational Amenorrhea Method (LAM):

The Lactational Amenorrhea Method (LAM) is a temporary contraceptive option for postpartum women.

Failure rate: 5- 40 /HWY.

Mechanism:

- Prolonged lactation causes increase in prolactin level (anti-gonadotrophic in action & release).
- To increase the efficacy of this method, there must be regular breast feeds with no supplementary feeds, so this method is effective & the best during the 1st six months.

Advantages of LAM:

- Available to all breastfeeding women.
- If all prerequisites are available it gives 98% effectiveness.
- Protection begins immediately postpartum.
- Other benefits of breast feeding.

Disadvantages of LAM:

- Difficulty to establish full breast feeding in all women.
- No STI or HIV protection.
- Temporary method (1st six months postpartum).

X. Family Planning

HORMONAL CONTRACEPTION

Types of Hormonal Contraceptives:

- o The Combined Oral Contraceptive (COC).
- o The Progestogen-Only Pill (Minipill).
- o Injectable Contraceptives.
- o Subdermal Contraceptive Implants.
- o Contraceptive Vaginal Rings.
- o Contraceptive Skin Patch.
- o Hormone-Releasing Intrauterine Devices.

Oral contraceptive pills

Types of oral contraceptive pills (OCS):

- o Combined oral contraceptives (COCS).
- o Progestin only pills (POPS).
- o Sequential Pills (obsolete nowadays, removed since 1976).

Combined oral contraceptives:

The commonest hormonal contraceptives and it contains estrogen and progesterone preparation.

Mode of action:

- o Inhibition of the ovulation (the main mechanism),
- Due to suppression of the pituitary and the hypothalamus i.e. decrease of GnRH and gonadotropins (estrogen action).

- o Effect on the endometrium:

Glandular atrophy and stromal edema (progesterone action). So, the endometrium becomes unsuitable for implantation.

Effectiveness of the OC (the most reliable method):

- o Theoretical failure rate: 0.1/HWY.
- o Practical failure rate: 1/HWY.

Types:

Combined fixed dose pills: (Monophasic pills).

- o Each packet contains 21 active pills with the same amount of E and P.
- o Each pill contains estrogen (Ethinyl Estradiol "EE") and progesterone.

According the estrogen dose they are classified into:

- o High dose pills containing 50 ug. Ethinyle estradiol
- o Low dose pills containing 30 ug Ethinyle estradiol
- o Lowest dose pills containing 20 ug Ethinyle estradiol

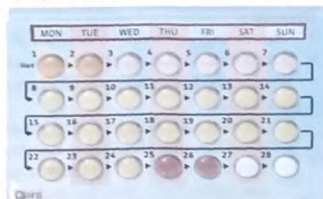
Progestins: There are 3 main groups:

First generation: Norethisterone.

Second generation: Levonorgestrel.

Third generation:

- Desogestrel (Marvelon)
Desogestrel 150 ug + EE 30 ug
- Gestodene (Gynera)
Gestodene 150 ug + EE 30 ug
- Norgestimate (Cilest)
Norgestimate 250 ug + EE 35 ug



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D. Fourth generation:

- Drospirenon: Yasmin (ethinylestradiol 30 µg/ drospirenone 3mg).
- Qlaira (estradiol valerate / dienogest in complex quadruphasic dosage regimen). continuous 28-day cycle of 26 active tablets followed by 2 placebo tablets; missed pill advice is complex.

2- Biphasic pills:

Estrogen dose is fixed for 21 days while progesterone dose is doubled in the last 14 pills.

3- Triphasic pills (Triovlar):

Designed to mimic the hormonal changes of the natural menstrual cycle. Ethinyl estradiol dose is 30 µg for 6 days, 40 µg for 5 days and 30 µg for 10 days. While levonorgestrel dose is 50 µg, 75 µg and 125 µg for corresponding days.

Advantages:

A) Contraceptive advantages:

- o No interference with sexual intercourse.
- o Available, reliable & reversible.

B) Non-contraceptive advantages:

- o Cycle regulation.
- o Relieves cyclic problems as premenstrual tension syndrome & spasmodic dysmenorrhea).
- o Therapeutic modality in endometriosis, fibroid, acne & hirsutism.
- o Decrease incidence of endometrial & ovarian carcinoma.
- o To postpone menstruation.

Disadvantages:

A) Related to method of administration:

Daily regular administration.

B) Related to effectiveness:

Some drug may reduce efficacy of the COC (enzyme inducers).

C) Related to side effects:

Gastrointestinal tract:

- Nausea and vomiting may occur due to gastric irritation by estrogen as well as its effect on the vomiting center. This is frequent in the first 3 months and tends to disappear by time.
- COC predisposes to gallstones, cholestatic jaundice, benign and malignant hepatoma.

Central nervous system:

- Headache and Mood changes as irritability and depression.

Breasts:

- Breast engorgement, tenderness or enlargement (estrogen & progesterone effects).
- Diminished milk secretion in lactating women(E).
- Prolonged use more than 10 years causes slight increase in breast cancer.

Genital tract:

- Menstrual disorders as hypomenorrhea, breakthrough bleeding and Amenorrhea.
- Breakthrough bleeding is common in the 1st 3 cycles either due to missing of pills or low hormone content. The latter is treated by taking 2 tablets daily until the bleeding stops, and then one tablet daily until the pack is finished. The extra pills should be taken from another pack.
- Amenorrhea and hypomenorrhea may be caused by endometrial atrophy due to progestogen.
- Increased normal vaginal discharge, i.e. leucorrhoea.
- Cervical erosion (ectopy) is common.
- Estrogen predisposes to Candida vulvitis and vaginitis.
- Increase in the size and red degeneration of uterine myomas.

X. Family Planning

Cardiovascular system:

- Mild hypertension occurs in about 5% of cases using high-estrogen tablets for more than 5 years. It is due to water and salt retention. Low-estrogen tablets have minimal effects on blood pressure.
- Changes may occur in blood coagulation predisposing to venous thrombosis and pulmonary embolism due to decreased antithrombin (natural anticoagulant) and increased platelet aggregation.
- Atherosclerosis (progesterone increases low density lipoprotein & decreases high density lipoproteins).

Metabolic effects:

- Increase in body weight due to water and salt retention, and due to anabolic effect of progesterone.
- On carbohydrates: hyperglycemia (estrogen increases glycogenolysis & progesterone increases insulin resistance).
- On lipids: increases LDL & decreases HDL predisposing to atherosclerosis (progesterone effect).

Skin changes:

- Skin pigmentation (chloasma).
- Acne vulgaris, hirsutism may appear with high progesterone content (androgenic) or improve with high estrogenic content.
- Anti-Cosmetic effect of COC includes acne, hair loss & weight gain.

Congenital fetal malformations:

- Women may continue to take contraceptive pills unaware that they are pregnant. This may cause enlargement of the clitoris and fused labia minora in the female child & VACTERL syndrome.

Contraindication of oral contraceptive pills:

A) Absolute contraindication

- Malignant hypertension.
- Thromboembolic disorders.
- Past-thrombo-vascular accidents.
- Active liver disease, cirrhosis and liver tumors.
- Pregnancy.
- Valvular heart diseases with complication.
- Unexplained vaginal bleeding.
- Breast cancer.
- Breastfeeding less than 6 weeks after childbirth.

B) Relative contraindication:

- Smokers especially if > 35 years.
- Mild and moderate hypertension.
- Prolonged immobilization.
- Gallbladder disease.
- Current treatment with antibiotics (rifampin, Griseofulvin) or antiepileptic's.
- Epilepsy.
- Breastfeeding women 6 weeks to 6 months after childbirth.
- Not breastfeeding during first 3 weeks after childbirth.

General instructions:

☐ **Before giving the pills:**

Full history and examination are essential to exclude any contraindications.

☐ **Administration:**

- ☐ The pills are started on any of the 1st 5 days of the menstrual cycle and given for 21 days. After a rest for 1 week, another pack is started. Withdrawal bleeding should start 2 or 3 days after stopping the tablets.

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- Some formulations add 7 iron tablets to be taken during the steroid-free week to guarantee continuous drug intake.

- **Missing a pill:**

- If one pill is missed, it is taken as soon as remembered and the next pill is taken in its time.
- If more than one pill are missed, 2 pills are taken when remembered & the next pill is taken in its time. It is advisable to use an additional method of contraception as the male condom for the rest of the cycle.
- If there is a cause of missed pills as vomiting or diarrhea, use extra-precautions during the illness.

- **Drug interaction:**

- Certain drugs reduce the efficacy of the combined tablets as sedatives, tranquilizers, antihistaminic drugs, antibiotics as penicillin & Rifampicin.

- **Relation to surgery:**

- Postoperative thrombosis is increased in women on COC.
- The patient should stop pills 4-6 weeks before & after major surgery.

2. **Mini pills "Progestogen only pills":**

It consists of a small dose of a progestogen as norethisterone or levonorgestrel.

Types:

- Micronor (Norethisterone).
- 2-Microlut (Levonorgestrel) (35 tablets).
- 3-Exluton (Lynestrenol) (28 tablets).
- 4-Cerazette (75 µg desogestrel).

Mechanism of action:

- Increase cervical mucus hostility (the main mechanism).
- Endometrial atrophy which is unsuitable for implantation.
- Inhibition of ovulation which occurs in about 50% of cases (97% in Cerazette).

Administration:

Daily without interruption starting on the 1st day of the menses at fixed time of the day, but Cerazette has 12 hours permission (minipills are given about 3-4 hours before the usual time of intercourse to give the maximum effect).

Indications:

- Lactating mother whose fertility is reduced by lactation, and also milk production is not affected.
- When estrogen is contraindicated. The mini pill has no effect on blood pressure or coagulation factors. Also, their effect on lipid metabolism and liver is minimal.
- Women who develop estrogen side effects while using COC.

Contraindications:

- Past history of ectopic pregnancy.
- History of irregular menses
- Progesterone allergy.

Disadvantages:

- Less effective than the combined tablet.
- Irregular uterine bleeding and amenorrhea are frequent.
- Headache, nausea, breast tenderness, mood changes, depression, acne, and diminished libido may occur.
- If pregnancy occurs, the incidence of ectopic pregnancy is increased. The progestogen decreases tubal motility.

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Injectable contraceptives

Types of injectable contraceptives:

1) Progestin-only injectables:

- Depo-Provera (medroxyprogesterone acetate).
- It is injected IM in a dose of 150 mg every 3 months.
- Subsequent injections must be given no more than 2 weeks early or 2 weeks late).

2) Combined injectable contraceptives:

- Composed of both estrogen and a progestogen.
- Estrogen is added to prevent irregular uterine bleeding.
- Injection is given IM every month (30 ± 3 days) either Mesygyna (50 mg norethisterone enanthate + 5 mg estradiol valerate) or Cyclofen (25 mg DMPA + 5 mg estradiol cypionate).

Indications:

- o Lactating women as it increases milk secretion.
- o When estrogen is contraindicated.
- o Women who develop estrogen side effects while using COC.
- o Women who regularly forget the tablet and are unable to tolerate the IUD.

Pregnancy rate:

About 0.3 per HWY.

Mechanism of action of injectable contraceptives:

- o Inhibition of ovulation.
- o Decrease tubal motility.
- o Atrophy of endometrium.
- o Increase cervical mucus hostility.

Advantages of injectable contraceptives:

Progestin-only injectables:

- o Safe and highly effective (more than 99%).
- o Long-acting, but reversible; can be discontinued without provider's help.
- o No daily or coital related use.
- o Have no effect on lactation and can be used by breastfeeding women.
- o Reduce the incidence of ectopic pregnancy (inhibit ovulation).

Combined injectables:

The same advantages as progestin only injectables in addition to:

- o Cause less menstrual disturbance than progestin-only injectables.
- o Return to fertility more rapid than progestin-only injectables.

Disadvantages of injectable contraceptives:

Progestin-only injectables:

- o Menstrual changes in the form of irregular
- o uterine bleeding and amenorrhea.
- o Fertility is delayed about 9 months after stopping the drug.
- o Weight gain, Headache, nausea, breast tenderness, mood changes, depression, acne, and diminished libido may occur.
- o Osteoporosis may occur due to the hypoestrogenic state, caused by sustained ovarian inhibition.

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Combined injectables:

- o Menstrual changes are present but less common than with progestin-only injectables.
- o Estrogen-related side effects.

Non-contraceptive health uses of progestin-only injectable contraceptives:

- o Endometriosis
- o Endometrial hyperplasia
- o Advanced and recurrent endometrial carcinoma
- o Precocious puberty
- o Hirsutism.

Time of Injections:

- Menstruating woman: Within the first 7 days (the first 5 days – FSRH) of the menstrual cycle, or at any time provided the woman is not pregnant. If given after day 7 (day 5), a male condom, or a contraceptive vaginal tablet is used for 48 hours (backup method).
- Lactating woman: Six weeks after delivery.
- Non-lactating woman: At any time during the first 6 weeks after delivery. No need to wait for menstruation to start.
- Abortion: Immediately, or within the first 7 days (5 days) after abortion.

Subdermal implants

These are the most recent contraceptive modalities introduced in the market.

Types:

A. Biodegradable implants:

Capron or (single biodegradable capsule releasing levonorgestrel).

B. Non-biodegradable:

2. The Norplant System:

- Six capsules containing levonorgestrel are inserted subcutaneously in the inner side of the upper arm in a fan-shaped manner using local anesthesia.
- Norplant prevents pregnancy for 5 years, and then the capsules are removed under local anesthesia.
- The mode of action and side effects are like Depo-Provera.
- The Norplant system has been withdrawn from UK because of the side effects.



The Two Rod System (Jadelle)

It consists of 2 solid rods. Pregnancy is prevented for 5 years.



3. Implanon:

It consists of one rod which contains 68 mg of etonogestrel which is released at a rate of 40 micrograms daily. It prevents pregnancy for 3 years.



Contraceptive vaginal rings

- These are rings containing hormones.
- The ring is inserted by the patient into the vagina.
- The hormones released are absorbed by lymphatics through the vaginal walls and bypass the liver, so the side effects are less compared with the oral tablets.



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Types:

1. The combined vaginal ring:

An example is the Nuva ring which releases ethinyl estradiol and etonogestrel. The ring is inserted into the vagina on the 5th day of the menstrual cycle and left for three weeks, then removed, and reinserted again after one week to allow withdrawal bleeding. It contains hormones to prevent pregnancy for one month. Failure rate is about 0.5 per HWY.

2. The progestogen-only vaginal ring:

It releases levonorgestrel. It is replaced every three months. It acts similar to progestogen-only pills. However, failure rate is high.

Contraceptive skin patch

The patch is applied to the skin for one week, and then replaced with a new one. Three patches are used for 3 weeks. The fourth week is patch free. Pregnancy rate is 1 per HWY.

INTRAUTERINE CONTRACEPTIVE DEVICE (IUCD OR IUD)

The IUD is an effective and safe method of contraception. All devices are made of polyethylene (plastic) which is not irritant to the tissues and is mixed with barium sulphate to be radio-opaque to confirm the presence of the device.

Types:

A) **Inert devices** made only of polyethylene and are called nonmedicated devices e.g. Lippes loop (not used nowadays).

B) Medicated devices:

- Copper devices which release copper.
- Hormone-releasing devices which release progesterone.

Copper devices:

The most commonly used at the present time and include:

Nova T (Novagard):

- The surface area of copper is 200 mm².
- The copper wire contains a silver core.
- Silver prevents fragmentation of copper and prolongs the life-span of the device which is 5 years.

□ Copper T380 A:

- Duration of action is 10 years. TCu-380 A is the most effective and most widely used all over the world.

□ Multiload Copper Devices:

- Multiload Cu-250. Duration of action is 3 years.

Hormone-releasing devices:

1. Progestasert:

It is a T-shaped plastic device. The vertical limb carries a silastic capsule which contains progesterone (38 mg). Action lasts for one year.

Levonorgestrel T device (Mirena):

- It is a T-shaped plastic device.
- The silastic reservoir contains levonorgestrel (52 mg) which is released at a rate of 20 Ug/day.
- Action lasts for 5 years.



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- It does not increase the rate of ectopic pregnancy.
- The pregnancy rate is less than 0.2 HWY.
- Disadvantages include high cost and progestogen side effects as headache, edema, mood changes, diminished libido and hirsutism.

Mode of action:

- It interferes with implantation by making the endometrium unsuitable for implantation. This foreign body reaction is more evident with the copper devices.
- It interferes with fertilization because copper ions inhibit sperm motility and capacitation.
- The device stimulates tubal peristalsis so the ovum reaches the uterine cavity before fertilization or before the endometrium is ready for implantation.
- It causes utero-tubal spasm preventing meeting of the ovum and spermatozoa.
- It stimulates uterine contractions, and thus may prevent implantation of the ovum but it does not cause abortion.
- The hormone-releasing device acts by making the endometrium atrophic and unsuitable for implantation, makes the cervical mucus thick, scanty, and viscid.

Side effects and complications:

Vasovagal syncope:

- Discomfort, Pain and even vasovagal syncope may occur during insertion

Bleeding:

- The most common problem.
- It may be in the form of post insertion bleeding, menorrhagia, or intermenstrual bleeding.
- Menorrhagia is frequent in the first 3 months after insertion. Menorrhagia is treated by oral antifibrinolytic agent as tranexamic acid and a prostaglandin inhibitor. Drugs which reduce capillary fragility and increase platelet aggregation as ethamsylate can be used.

Vaginal discharge:

- Most patients will have a slight watery or mucoid discharge due to mechanical irritation of the endometrium and endocervix.

Pain:

- The patient may complain of different types of pain as uterine colic, pelvic discomfort, lower abdominal pain, low backache and congestive dysmenorrhea (due to pelvic congestion).
- Pain is less with the hormone-releasing device due to the inhibitory effect of the hormone on the myometrium.

Pelvic infection:

- Acute and chronic salpingitis

Perforation of the uterus.

- It usually occurs at the time of insertion.

*** Factors which predispose to perforation:**

- The skill of the gynecologist and the mode of insertion.
- Acute antelexion or retroflexion of the uterus.
- Soft uterus after abortion or labour.
- Presence of a uterine scar as after caesarean section.

*** Perforation is suspected in the following situations:**

- Occurrence of severe pain or abnormal bleeding at the time of insertion.
- Persistence of pain or bleeding after insertion.
- Development of pelvic infection.
- Disappearance or shortening of the threads.

*** If perforation is suspected and pregnancy is excluded:**

- confirm the position of the device by doing ultrasound scan for the cavity and the wall.

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- If not found by ultrasound, a plain abdominal x-ray is taken. If the device is not seen it means that it has been expelled. If it is seen in the mid or upper abdomen, this indicates that it has perforated the uterus but if seen in the pelvis we cannot be sure that it is inside or outside the uterus.
- In case of perforation the device should be removed as early as possible. Removal is carried out by laparoscopy or laparotomy.
- o **Expulsion:**
 - Most of the expulsions (50%) occur in the first 3 months after insertion, mostly during menstruation.
- o **Pregnancy:**
 - The pregnancy rate is 0.5 to 3 per hundred women in the first year of application and gradually falls in subsequent years.
 - If pregnancy occurs, the device should be removed immediately if the threads are visible to avoid complications in the form of abortion (about 50%), preterm labour (20%) and infection.
 - Removal should be done immediately before pregnancy advances as the device becomes drawn upward into the uterine cavity.
 - The presence of the loop does not increase the rate of congenital fetal malformation if accidental pregnancy occurs.
- o **LNG intrauterine system:**
 - Hormonal side effects due to systemic absorption of LNG (headache, mood changes and mastalgia).
 - There is slight increase in incidence of functional ovarian cysts in comparison to COC.

Contraindications:

- o Suspected pregnancy.
- o Pelvic infection as vaginitis, cervicitis and salpingitis.
- o Uterine malformation as bicornuate uterus.
- o Menorrhagia or unexplained vaginal bleeding.
- o Fibroids distorting the uterine cavity.
- o History of ectopic pregnancy or persistent GTD.
- o Recent hysterotomy or CS and early puerperium for fear of perforation.
- o Coagulopathy and anticoagulant therapy (Mirena can be used).
- o Valvular heart disease. There is a risk of bacterial endocarditis as the organisms may be introduced during insertion or removal of IUD. However, an antibiotic as Ampicillin 2 grams can be taken orally one hour before insertion or removal.

Technique of insertion:

- The loop is inserted immediately after menstruation or on the last day when the cervix is still open and to be sure that there is no pregnancy. However, it can be inserted at any time during the menstrual cycle, provided the woman is not pregnant.
- Usually, no anesthesia is required.
- The patient is placed in the lithotomy position and examined bimanually to know the size and position of the uterus and to exclude the presence of a contraindication to insertion as bicornuate uterus or the presence of fibroids.
- A Cusco speculum is inserted to expose the cervix, which is cleaned with antiseptic solution, and then grasped by the vulsellum to steady and straighten the uterus.
- A uterine sound is passed to determine the length and direction of uterus.
- Insertion is via the withdrawal techniques. Used for copper devices. The inserter is introduced to reach near the fundus of the uterus with the piston fixed below the threaded device, and then the outer sheath is withdrawn externally. This technique reduces the incidence of uterine perforation.

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Instructions of the patient:

- The woman is informed about the type of IUCD to be used, its duration of action, and the date of replacement.
- The woman is told that menorrhagia is frequent during the first 3 months following insertion.
- The woman is instructed to examine herself periodically and routinely after each period to feel the threads to be sure that the device is in place.
- She should report if threads are not felt, if a period is missed, or there is severe pelvic pain and fever to exclude pelvic infection.

Causes of missing thread:

- o Expulsion of loop.
- o Perforation of uterus.
- o Pregnancy.
- o The loop may be displaced upside down.
- o Threads cut too short.
- o Threads withdrawn inside the cervical canal.
- o Detachment of the threads.
- o Threads becoming adherent to vagina by thick mucus.

Non-contraceptive benefits:

LNG IUS decreases blood loss and pain, so can be used in management of heavy menstrual bleeding, endometriosis and adenomyosis.

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BARRIER METHODS OF CONTRACEPTION

□ *The male condom:*

It is made of latex rubber. Condoms lubricated with a spermicide as nonoxynol-9 are more effective than condoms without spermicide.

Disadvantages:

- It interferes with full genital contact so the act is less pleasurable.
- May interfere with erection.
- Allergic reaction to latex or spermicide may occur in both partners.
- Failure rate is 6-21 per HWY

Advantages:

- Technique is simple.
- Avoids sexually transmitted diseases.
- Protects against carcinoma of cervix.
- Medically safe.

The female condom (femidom):

- It is a polyurethane sheath which lines the vagina.
- It is 15 cm long and 7 cm wide.
- It has an internal flexible ring at the closed end which covers the cervix and an external ring which remains outside the vagina, and partially covers the vulva.
- It is for single use only and it is stronger than male condom.



Vaginal diaphragm:

- It is dome-shaped, made of rubber or latex and with a flexible metal rim.
- There are different sizes. The proper size is known by trying different caps and it must fit well against the vaginal walls all around.
- A spermicidal cream is placed in the dome of the diaphragm next to the cervix and smeared round the edge.
- The cap is inserted by the woman before intercourse and is not removed except at least 8 hours after the act so that all the spermatozoa will be killed by vaginal acidity.



Cervical cap:

- It is cup-shaped, made of rubber and fits directly over the cervix where it is retained by suction and its flexible rim.
- A contraceptive cream must be placed in the cup and smeared around the edge.
- It is difficult to apply and to remove, it cannot be applied if the cervix is lacerated and may be displaced during coitus.
- It is removed at least 8 hours after coitus.



The vaginal sponge:

It is a synthetic polyurethane sponge containing one gram of nonoxynol-9 which kills sperms. It fits into the upper vagina and covers the cervix. It acts both as a mechanical and a chemical contraceptive. It is removed at least 8 hours after intercourse.



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CHEMICAL CONTRACEPTIVES (SPERMICIDES)

- In the form of vaginal tablets, creams, jellies containing a spermicidal drug as nonoxynol-9 which causes cosmetic changes in the sperms leading to its death.
- Applied 15-30 minutes before intercourse.
- They are unreliable, failure rate about 20-25 per HWY and may cause chemical vaginitis or cervicitis, so may increase the risk of HIV transmission.
- They are not used alone but with the condom or vaginal diaphragm to improve their efficacy.

POSTCOITAL CONTRACEPTION (EMERGENCY CONTRACEPTION)

Postcoital contraception is not considered an abortifacient because pregnancy begins at implantation not at fertilization.

Indications:

- Unprotected sexual intercourse at any time during the menstrual cycle.
- Rape.
- Failure of barrier methods, as when the condom ruptures.

Methods:

1- Hormones:

These are given immediately after intercourse or maximally within 72 hours (the morning-after pill).

Hormones include:

A. The combined estrogen-progestogen tablet:

- This is known as **Yuspe regimen**.
- If we use a high-dose tablet, 2 tablets are given and repeated after 12 hours. If we use a low-dose tablet, 4 tablets are given and repeated after 12 hours.

B. The progestogen-only pill:

- **Contraplan II** pill contains 750 micrograms of levonorgestrel, so one tablet is given within one hour of coitus, and repeated after 12 hours, but can be used up to 72 hours.
- The minipill is associated with less nausea and vomiting and is more protective compared with the combined pill.
- With a history of thrombosis, the progestogen-only regimen is preferred.

C. Ulipristal acetate:

- It is selective progesterone receptor modulator (SPRM) which is as effective as levonorgestrel but used up to 120 hours.

Mode of action of the morning-after pill:

It is not clear; however, it may be through inhibition of ovulation or rendering the endometrium unsuitable for implantation.

Side effects:

- Nausea and vomiting may occur.
- Antiemetic can be taken one hour before the first dose.
- If vomiting occurs in less than one hour we repeat the dose.
- These complications are less with the minipill

Efficacy:

Pregnancy rate with the progestogen-only pill is about 1%; it is 2-3% with the combined tablet, while it is 1% with IUCD.

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2- Mechanical methods:

An intrauterine contraceptive device is inserted immediately or up to 5 days after intercourse. It may act by preventing implantation.

3- Old methods (*Very less likely to be successful*)

Douching after intercourse:

- To wash away the sperms before entering the cervix.
- Fluids used are simple water or spermicidal solution as dilute acetic acid which is acidic.
- Failure rate is high because semen may be ejaculated directly into the cervical canal.
- It can be used as an emergency method as when the condom breaks.

Menstrual aspiration:

Menstrual aspiration is done using a special cannula (Karman cannula) and a 50-ml syringe to aspirate the uterine contents. Procedure is performed one week after intercourse or 1-3 weeks after a missed period.

SURGICAL METHODS FOR CONTRACEPTION

1- Female:

A) Tubal sterilization.

B) Hysterectomy.

Tubal sterilization:

- **Laparoscopy:**
 - **Fulguration:** By electrocauterization.
 - **Clips:** Hulka & Filshie clips destroy 3 – 4 ml respectively of Fallopian tube.
 - **Rings:** Falope ring destroys 2.5 ml of fallopian tube.
 - **Laser beam.**
- **Mini-laparotomy:**
 - **Madlener:** Crushing & ligation of a tubal loop by non-absorbable suture.
 - **Irving:** Excision of part of tube, then the medial end is embedded into myometrium & the lateral end between the two layers of broad ligament.
 - **Cook:** As Irving, but the medial end in round ligament.
 - **Uchida:** As Irving but the medial end in broad ligament.
 - **Pomeroy:** A loop of the tube is isolated, double ligated then it is cut.
 - **Parkland:** Mesosalpinx is perforated in avascular area & the tube is ligated by chromic 0 & segment of the tube is excised.
- **Hysteroscopy:**
 - A type of operative hysteroscopy, in which the tube is occluded by:
 - Electrocautery after visualization of both ostia.
 - Cryodestruction.
 - Injection of sclerosing material in the tubes.
 - Injection of quinacrine or silicon rubber inside the tube which when harden form plug filling 2/3rd of the tube taking its shape, it is reversible as it can be removed by hysteroscopy, but very difficult with high failure rate (ectopic pregnancy if not all lumen is occluded).
 - Essure Microinsert system is a permanent contraception in which an implant is placed into each tube which involves an occlusion without anesthesia.

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Posterior colpotomy:

- An incision is made in the posterior vaginal fornix followed by opening of the peritoneum of Douglas pouch. The tubes are pulled out and occluded.

Indications of sterilization:

- o Medical disorder that may threaten the patient's life if pregnancy occurs.
- o A patient with repeated cesarean sections especially if more than 4.
- o Genetic disease transmissible to the fetus.
- o Failed other contraceptives in a patient with adequate number of children.

Advantages of female sterilization:

- o Very safe and highly effective (99.5% in first year of use, 98.1% overall for 10 years of use).
- o Permanent method.
- o Virtually no long-term adverse effects.

Disadvantages of female sterilization:

- o A small risk of surgical complications such as injury to other organs, infection or bleeding
- o Offers no protection against STIs, including HIV.
- o Cannot be reversed should the woman change her mind.
- o Can have a relatively high initial cost.

Timing of female sterilization:

- Immediately or within the first 7 days after a vaginal delivery (postpartum).
- During CS.
- At any other time between pregnancies except between the 7th day following delivery and 4 to 6 weeks after delivery.

Complications of tubal sterilization:

I. Early complications:

- o **Complications of anesthesia:**
 - laryngeal spasm,
 - Cardio-vascular accidents,
 - convulsions and
 - vomiting
- o **Injury to important structures:**
 - bowels,
 - urinary bladder,
 - pelvic part of ureter and
 - pelvic colon.

Hemorrhage:

- Bleeding may occur from the cut ends of the tube,
- treated by cauterization of the cut ends.

Shock

Failure of the technique.

II. Remote complications:

o Infections:

- Generalized or localized peritonitis,
- wound infection, and
- pulmonary complications.

o Menstrual disturbance:

- o E.g. Menorrhagia and polymenorrhea due to chronic pelvic congestion

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- *Hydrosalpinx and pyosalpinx.*
- *Ectopic pregnancy.*
- *Peritoneal and omental adhesions.*

2- Male sterilization:

1-vasectomy:

- Voluntary male sterilization, or vasectomy, is a minor surgery in which the vas deferens are tied and cut to prevent sperms from mixing with the seminal fluid.
- Ejaculated semen that does not contain sperms cannot fertilize and ovum.
- Vasectomy is not immediately effective. A waiting period of 12 weeks or 20 ejaculations is recommended before couple can rely on vasectomy to prevent pregnancy.



2- Intravasal occlusion device (IVD) and plugs.

Contraception in the elderly Patient (above 40 years):

Methods:

- The combined oral contraceptives containing low-dose estrogen (20 or 30 ug). They can be used in women over 40 years and until the menopause
- The progestogen-only pill.
- The barrier methods.

POSTPARTUM CONTRACEPTION

Methods:

- Breast-feeding. Lactational amenorrhea can be used as a method of contraception, provided certain criteria are fulfilled as mentioned before.
- The progestogen-only pill.
- Injectable progestogens as Depo-Provera.
- Subdermal contraceptive implants.
- Intrauterine contraceptive device.
- Barrier methods.
- Postpartum sterilization. It is done on the same day or at most 2-3 days after delivery, when the uterus is still high in the abdomen.

Progestogen-only contraceptive methods:

- The progestogen-only pill.
- Injectable progestogens as Depo-Provera.
- Subdermal contraceptive implants.
- Progesterone and levonorgestrel releasing intrauterine device.
- The progestogen-only (levonorgestrel) vaginal ring.

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Choice of the contraceptive method

The ideal contraceptive method should be:

- ✓ 100% effective,
- ✓ Easy to use,
- ✓ Completely reversible,
- ✓ Does not delay return of fertility;
- ✓ Totally acceptable,
- ✓ Absolutely free of side effects,
- ✓ Inexpensive,
- ✓ Widely available and
- ✓ Preferably not related to sexual intercourse.

No such method exists!! However,

- The combined contraceptive pill is the most reliable method.
- For the newly married couple, advise the pill or the condom.
- For the multipara, advise the pill or IUD or a barrier method.
- For the lactating woman, the best is IUD or a barrier method. The mini-pill or Depo-Provera or contraceptive implants as Norplant can also be prescribed.
- Sterilization may be considered in some cases.

Recent contraceptives (under trial):

- **Mifepristone (Ru 486):**

Synthetic non-steroid, progesterone antagonist at the level of the receptors.

- **Immunological method:**

by Contraceptive vaccines as anti-hCG vaccine, anti-zona pellucida vaccine and anti-sperm vaccine.

- **Male pills:**

e.g. gossypol which inhibits spermatogenesis.

XI. Legal Aspects in Gynecology

Female Genital Cutting

Definition:

Female genital cutting (FGC), also called female genital mutilation (FGM) comprises all procedures that involve partial or total removal or injury of the female external genitalia, clitoris, labia minora and/or majora that is commonly called in public slang female circumcision (although it differs totally from male circumcision).

Epidemiology:

FGC is mostly carried out on young girls sometime between infancy and adolescence, and occasionally on adult women. More than 200 million girls and women alive today have been cut in 30 countries in Africa, the Middle East and Asia where FGC is concentrated and over 3 million girls are estimated to be at risk of FGC annually.

FGC is highly concentrated in a group of countries extending from the Atlantic coast to the Horn of Africa, in areas of the Middle East and in some Asian countries like Indonesia as well as among migrants from these areas with wide variations in prevalence (see figure 1). The practice is almost universal in Somalia, Guinea and Djibouti, with levels around 90 per cent, while it affects only 1 per cent of girls and women in Cameroon and Uganda. FGC is therefore a global concern

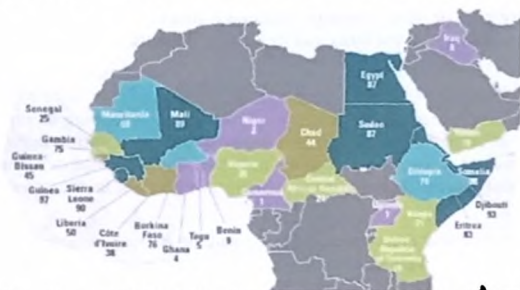


Fig. 1. Prevalence of FGC in Girls and Women aged 15-49 in Africa, UNICEF 2016

Legal & Human Rights issues

FGC is recognized internationally as a violation of the human rights of girls and women. It reflects deep-rooted inequality between the sexes, and constitutes an extreme form of discrimination against women. It is nearly always carried out on minors and is a violation of *the Egyptian constitutional rights of children*, the person's rights to health, security and physical integrity, and the right to life when the procedure results in death. Owing to this and to its harms, the procedure has been condemned by the Egyptian law considering it a crime.

Causes behind FGC

Causes given by people to justify the practice of FGC are diverse:

- Being a cultural tradition,
- a social norm like everyone else,
- to increase the girls' marriageability,
- to promote cleanliness and
- to ensure premarital virginity and marital fidelity are among the causes.

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Some believe that the practice has a religious support although religious leaders in Egypt including **Al-Azhar, Dar Al-Ifiaa' and the Egyptian church** have a uniform position against FGC that is declared as unfounded and even prohibited from a religious point of view.

Function of External Genitalia

The external genital organs include the mons pubis, labia majora, labia minora, Bartholin glands, and clitoris. The area containing these organs is called the vulva. The external genital organs have three main functions:

- Enabling sperm to enter the body
- Protecting the internal genital organs from infectious organisms
- Providing sexual pleasure
- Directs the urine in a stream by the labia minora preventing splashing and soiling of the vulva

Sexual Desire and the Sexual Response Cycle

Sex starts with desire in response to various stimuli like vision, sound, smell, memory, etc... Desire is a purely mental process that originates in the brain (not in external genital organs) and is influenced by personal, cultural, ethical and social factors. Sexual desire may or may not progress to the next phases of the sexual response cycle i.e. arousal, plateau, orgasm then resolution phases which are the physical reactions to sexual desire.

Role of the Clitoris and Labiae

These organs are very rich of nerve endings that make them extremely sensitive organs. Touch stimulation of the nerve endings in the labia and especially the clitoris produces sensations of sexual pleasure and orgasm.

The Real Reason behind FGC

This procedure is practiced by removal of sexually sensitive organs leading to suppression of female sexuality to decrease the sexual sensation and pleasure on a false assumption that this will protect the girl from being indulged in a premarital relationship protecting her chastity, fidelity and virginity. Again ***desire is a mental process that originates in the brain and not in the external genital organs.***

Historical Facts

Clitoridectomy is not something that is peculiar to Islamic or African countries. It had been practiced almost in every culture. In Germany an instrument used for excision for clitoral hypertrophy (Fig. 2) was provided by the German surgeon Johann Schultes (1595-1645).

Isaac Baker Brown was a British gynecology surgeon who advocated certain surgical procedures, including clitoridectomy as a treatment for insanity, epilepsy, catalepsy and hysteria and claimed a success rate of 70% (1850s)

In the beginning of the 19th century, in Australia, FGC was practiced in kindergartens. The procedure was claimed to stop masturbation, reduce women's mental disorders, cure female complaints and prevent or stop nymphomania.

Also in the beginning of the 19th century, publications on female circumcision appeared in American medical journals calling for performing FGC on the assumption that many neuroses, psychoses and other diseases have their origin in pathological conditions of the hood of the clitoris. The procedure was present in the American surgical textbooks till 1960s.

Clitoridectomy was performed in the West on alleged medical grounds to prevent masturbation and to cure nymphomania and other diseases, thus ***It disappeared*** once it was realized that this assumption is wrong. In the East, it is performed to emphasize a passive gender role and this is the reason for its continuation.



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Classification of FGC

Female genital cutting is classified into 4 major types.

Type I: Often referred to as **clitoridectomy**, this is the partial or total removal of the clitoris and/or the prepuce.

Type II: Often referred to as **excision**, this is the Partial or total removal of the clitoris and the labia minora, with or without excision of the labia majora.

Type III: Often referred to as **infibulation**, this is the narrowing of the vaginal opening through the creation of a covering seal. The seal is formed by cutting and repositioning the labia minora, or labia majora, sometimes through stitching, with or without removal of the clitoris.

Type IV: This includes all other harmful procedures to the female genitalia for non-medical purposes, e.g. pricking, piercing, incising, scraping and cauterizing the genital area.

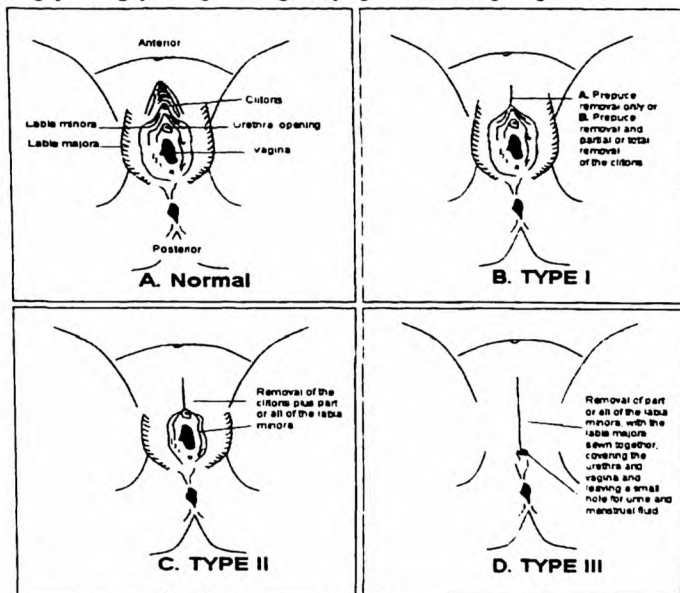


Fig. 3: Types of FGC

Complications and Health Hazards

FGC has no health benefits, and it harms girls and women in many ways. It involves removing and damaging healthy and normal female genital tissue, and interferes with the natural functions of girls' and women's bodies. Generally speaking, risks increase with increasing severity of the procedure.

These complications can be physical, sexual, obstetric and psychosocial complications.

Immediate complications

- Severe pain
- Excessive bleeding (hemorrhage)
- Genital tissue swelling
- Infections e.g., cellulitis, vulval abscess (Fig. 4), hepatitis C and tetanus.
- Urinary retention

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- Injury to surrounding genital tissue
- Fracture dislocation of bones and joints (child struggle)
- Hemorrhagic shock
- Neurogenic shock
- Death.



Figure 4. Clitoral cyst for healing in type III



Fig 5. Girl legs are tied to allow



Fig 6. Infection and disfigurement

Long-term consequences

- Scarring leading to ugly look, urethral stricture, labial fusion and keloid
- Urinary problems (painful urination, urinary tract infections)
- Increased risk of childbirth complications like difficult delivery, excessive bleeding, tears and lacerations, caesarean section, need to resuscitate the baby and newborn death
- Need for later surgeries: for example, the FGC procedure that seals or narrows a vaginal opening (type III) may need to be cut open later to allow for sexual intercourse and childbirth. Sometimes genital tissue is stitched again several times, including after childbirth, hence the woman goes through repeated opening and closing procedures, further increasing both immediate and long-term risks.

Psychological problems

- Post-traumatic stress disorder
- Anxiety
- Depression
- Low self-esteem

Long term sexual problems

- Fear of sexual intercourse
- Vaginismus which is the involuntary spasm or contraction of muscles around the vagina whenever penetration is attempted preventing it.
- Dyspareunia (pain during intercourse)
- Decreased sexual pleasure and satisfaction
- Frigidity
- Anorgasmia

The Situation of FGC in Egypt

Egypt is classified as a 'very high prevalence' country. The demographic health surveys (DHS) showed that the prevalence of FGC among "ever married" women between 15 and 49 years of age was 97% in 2000 that dropped to 92.3% in 2014. Among "all" women between 15 and 49 years, it was 91% in DHS 2000 but dropped to 87.2% in Egypt health issues survey (EHIS) 2015.

The practice was mostly carried out by traditional circumcisers, who often play other central roles in communities, such as attending childbirths (Doulas or Dayas). In many settings, health care

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providers perform FGC due to the erroneous belief that the procedure is safer when medicalized. Studies showed that Type II is the most commonly practiced in Egypt with 77% of women studied had partial or total removal of the clitoris and 60% includes also the labia minora.

However, activities against FGC lead to a more encouraging picture when we examine the DHS data on Egyptian girls aged 0-17 between 2005 and 2015, which concludes that the total percentage of girls who had already undergone FGC and those who were likely to undergo it before they reached 18 years of age **fell from 69% to 55%** in that Period and this reflects the positive attitude and response in the society.

Medicalization of FGC in Egypt and its Consequences on the Society and on the Practicing Physician:

Medicalization of FGC is the situation in which FGC is practiced by any category of health-care providers, whether in a public or private clinic, at home or elsewhere.

The Egyptian DHS showed that as the prevalence of FGC is declining, medicalization of FGC is rising. In 1995 survey FGC was practiced by a doctor in 45.8% of cases that rose to 74% in 2014 survey.

Medicalization of FGC in Egypt is becoming a problem in the society as it gives the practice a medical cover, thus, the procedure gets a false medical legitimacy in the society. People perceive doctors as persons who do no harm so they get a false sense of security, while, even practicing it with the most imminent physician will not prevent its long-term, psychological and sexual complications.

It is important to emphasize that practicing FGC by a physician is a violation of the Egyptian law and code of medical ethics and subjects the physician to grave consequences due to the following reasons:

- FGC is prohibited by the Egyptian law and is classified as a **crime** that subjects the person who practices it to **5-7 years in jail** (Amendment to Article 242 bis of Penal code, 2016).
- FGC is harmful and is **not a medical procedure** that requires the interference of a physician and its practice is prohibited by a **ministerial decree** since 2007.
- Dar Al-Iftaa' in 2006 has issued a fatwa saying "Female circumcision causes much physical and psychological harm, so, it **must be forbidden**".
- Harming a person is **against the medical ethical code of conduct** (do no harm).

Summary

- FGC includes removal or injuring the clitoris, labia minora and/or labia majora.
- Egypt has one of the highest prevalence of FGC worldwide that started to decline in the younger generation.
- It is practiced with the aim of suppressing women's sexually
- FGC has many short- and long-term health consequences both on the physical, psychological and sexual well-being as infection, bleeding, shock, death, scars, cysts, psychological distress, obstetric complications and sexual dysfunction.
- FGC is mostly carried out on young girls between infancy and age 15 and is considered as a violation of the human rights of girls and women.
- FGC is prohibited by Al-Azhar and Dar Al-Iftaa' owing to its harms.
- Practicing FGC is criminalized by the Egyptian law and the practitioner is imprisoned for 5-7 years.

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Bio Ethics

I-Medical ethics

Medical ethics is the disciplined study of morality in medicine it include.

1-DUTIES OF PHYSICIANS IN GENERAL

A PHYSICIAN SHALL:

1. Always exercise his/her independent professional judgment and maintain the highest Standards of professional conduct.
2. Respect a competent patient's right to accept or refuse treatment.
3. Not allow his/her judgment to be influenced by personal profit or unfair discrimination
4. Be dedicated to providing competent medical service in full professional and moral independence, with compassion and respect for human dignity.
5. Deal honestly with patients and colleagues, and report to the appropriate authorities those physicians who practice unethically or incompetently or who engage in fraud or deception.
6. Not receive any financial benefits or other incentives solely for referring patients or prescribing specific products.
7. Respect the rights and preferences of patients, colleagues, and other health professionals.
8. Recognize his/her important role in educating the public but should use due caution in divulging discoveries or new techniques or treatment through non-professional channels.
9. Certify only that which he/she has personally verified.

2-DUTIES OF PHYSICIANS TO PATIENTS

A PHYSICIAN SHALL:

1. Always bear in mind the obligation to respect human life.
2. Act in the patient's best interest when providing medical care.
3. Owe his/her patients complete loyalty and all the scientific resources available to him/her.
4. Whenever an examination or treatment is beyond the physician's capacity, he/she should consult with or refer to another physician who has the necessary ability.
5. A PHYSICIAN SHALL respect a patient's right to confidentiality
6. Give emergency care as a humanitarian duty unless he/she is assured that others are willing and able to give such care.
7. In situations when he/she is acting for a third party, ensure that the patient has full Knowledge of that situation.
8. Not enter into a sexual relationship with his/her current patient or into any other abusive or exploitative relationship.

3-DUTIES OF PHYSICIANS TO COLLEAGUES

A PHYSICIAN SHALL:

1. Behave towards colleagues as he/she would have them behave towards him/her.
2. NOT undermine the patient-physician relationship of colleagues in order to attract patients.
3. When medically necessary, communicate with colleagues who are involved in the care of the same patient.
4. This communication should respect patient confidentiality and be confined to necessary information

II-BASIC PATIENT RIGHTS

1. Access to emergency services
2. Participate in the development and implementation of care.
3. Be treated with respect and dignity
4. Be informed about condition, treatment options, and the possible results and side effects of treatment.

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5. Refuse treatment in accordance with the law, and receive information about the refusal of treatment.
6. Quality health care without discrimination because of race, creed, gender, religion or source of payment
7. Privacy and confidentiality, which includes access to medical records upon request
8. Personal safety.
9. Know the identity of the person treating the patient.
10. Informed consent for all procedures including participation in research, and recording by any mean.
11. Information, including the medical records by the patient or by the patient's legally authorized representative and hospital charges.
12. Consultation and communication.
13. The right to participate in end-of-life decisions
14. Complain or compliment without the fear of retaliation or compromise of access or quality of care.

III- Healthcare quality and Patient Safety

- The Centers for Medicare and Medicaid Services (CMS) defines healthcare quality as "the right care for every person every time."
- Patient safety is the avoidance and prevention of patient injuries or adverse events resulting from the processes of healthcare delivery (AHRQ)

WHAT IS MEDICAL ERROR?

Failure to complete a planned action as intended or, the use of a wrong plan to achieve an aim. "Doing the wrong thing when meaning to do the right thing."

ADVERSE EVENT

Unintended injury or complication which results in disability, death or prolonged hospital stay and caused by health care management rather than the disease process.

Maternal near miss definition

The WHO defines a maternal near-miss case as "a woman who nearly died but survived a complication that occurred during pregnancy, childbirth or within 42 days of termination of pregnancy."

Sentinel Event

An unexpected & unintended occurrence of death or loss of organ or permanent loss of function, not related to the natural course of the patient's illness or underlying condition.

Examples of Events Considered "Sentinel" by the Joint Commission

1. Suicide of any patient receiving care, treatment, and services in a staffed around-the-clock care setting or within 72 h of discharge, including from the hospital's emergency department (ED).
2. Unanticipated death of a full-term infant.
3. Discharge of an infant to the wrong family.
4. Abduction of any patient receiving care, treatment, and services.
5. Any elopement (i.e. unauthorized departure) of a patient from a staffed around-the-clock care setting (including the ED) leading to death, permanent harm, or severe temporary harm to the patient.
6. Hemolytic transfusion reaction involving administration of blood or blood products having major blood group incompatibilities (ABO, Rh, other blood groups).
7. Rape, assault (leading to death, permanent harm, or severe temporary harm), or homicide of any patient receiving care, treatment, and services while on site at the hospital or any staff member, licensed independent practitioner, visitor, or vendor while on site at the hospital.

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8. Invasive procedure, including surgery, on the wrong patient, at the wrong site, or that is the wrong (unintended) procedure
9. Unintended retention of a foreign object in a patient after an invasive procedure, including surgery.
10. Severe neonatal hyperbilirubinemia (bilirubin > 30 mg/dL)
11. Prolonged fluoroscopy with cumulative dose > 1,500 rads to a single field or any delivery of radiotherapy to the wrong body region or > 25% above the planned radiotherapy dose.
12. Fire, flame, or unanticipated smoke, heat, or flashes occurring during an episode of patient care.
13. Any intrapartum (related to the birth process) maternal death or *severe maternal morbidity*

Medical malpractice

Negligent conduct:

A physician's deviation from the applicable standard of care that a similar physician would exercise under the same circumstances (Omission /Commission).

Professional liability

The legal obligation of health care professionals or their insurers to compensate patients for injury or suffering caused by acts of omission or commission.

Professional liability formula

Duty +Breach of duty +Causation +Damages =LIABILITY

Steps to Minimize Medical malpractice:

- Practice within standard of care (Guidelines, Protocols & Clinical pathway)
- Stay current (KSA).
- Informed Consent.
- Early intervention.
- Documentation.
- Learn to trust the laws of physics.
- Avoid shortcuts
- Benchmark
- Proper Communications ,
- Clarity of job description & plan of Care.
- Rules & Regulations.
- Emergency drills.
- Training and retraining: Train for the worst and hope for the best.

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